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Section of Otology

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[*May* 3, 1935, *continued*]

The Treatment of Otosclerotic and Similar Types of Deafness by the Local Application of Thyroxine

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(*This Investigation was carried out at the Ferens Institute, Middlesex Hospital*)

ABSTRACT.—The treatment described is the rational sequence, dependent on the writer's vasomotor explanation of otosclerosis. It consists in the local application of thyroxine to the ear. Many years ago it was observed by the writer that thyroid extract applied locally to the mucous membrane of the nose produced an active congestion without inflammatory reaction and lasting for a long time. If otosclerosis is the result of a defective vasomotor response in the small blood-vessels of the ear, then thyroxine locally applied might overcome this defect.

Fourteen cases were treated and very considerable improvement resulted in seven of these (50%). Of these seven, tinnitus was greatly relieved in those in which that symptom was present. Wax also began to be secreted again. The subjective symptom of paracusis, usually considered of very unfavourable significance, is no contra-indication to this method of treatment, as two of the most successful cases were the subjects of paracusis.

The method of application is very simple and is described in full in the paper.

Cases which are not suitable for this treatment are very advanced cases, and those in which there is any serious loss of bone conduction, or in which the loss of hearing for high notes is marked.

RÉSUMÉ.—Le traitement décrit ici est la conséquence rationnelle de l'explication vasomotrice de l'origine de l'otosclérose donnée par l'auteur. Il consiste en l'application locale de thyroxine à l'oreille. Il y a des années, l'auteur observa que l'extrait de glande thyroïde appliqué localement à la muqueuse du nez produit une congestion active de longue durée, sans réaction inflammatoire. Si l'otosclérose est due à une réaction vasomotrice défective, la thyroxine appliquée localement pourrait surmonter ce défaut.

Quatorze cas furent traités par cette méthode, avec une amélioration considérable dans sept cas (50%). Parmi ces sept cas les bourdonnements d'oreille furent considérablement soulagés chez ceux qui présentaient ce symptome. La sécrétion de cérumen recommença aussi. Le symptome subjectif de paracousie, généralement considéré comme très défavorable, n'est pas une contreindication pour ce traitement, car deux des meilleurs résultats furent obtenus chez des sujets affectés de paracousie.

La méthode d'application, qui est décrite en détail dans l'article, est très simple.

Les cas auxquels ce traitement ne convient pas sont les cas très avancés, ceux avec une perte sérieuse de conduction osseuse ou de perception pour les tons élevés.

ZUSAMMENFASSUNG.—Die beschriebene Behandlungsmethode ist die rationelle Folge der von Verf. gegebenen vasomotorischen Erklärung der Entstehung der Otosklerose. Sie besteht in der lokalen Applizierung von Thyroxin an das Ohr. Vor vielen Jahren beobachtete Verf., dass die lokale Applizierung von Schilddrüsenextrakt auf die Nasenschleimhaut eine langdauernde aktive Hyperämie ohne entzündliche Reaktion verursachte. Wenn die Otosklerose Folge einer mangelhaften vasomotorischen Reaktion ist, so könnte die lokale Applizierung von Thyroxin diese Störung beheben.

Vierzehn Fälle wurden auf diese Weise behandelt, hier wurde bei sieben (50%) eine sehr beträchtliche Besserung erzielt. Bei diesen sieben Fälle, in denen Ohrgeräusche bestanden wurden diese erheblich vermindert. Auch Wachssekretion setzte wieder ein. Paracusis, ein subjektives Symptom, das gewöhnlich prognostisch sehr ungünstig gewertet wird, ist keine Kontraindikation für diese Behandlung, denn bei zwei der erfolgreichsten Fällen bestand dieses Symptom.

Die Technik der Behandlung, die in der Mitteilung ausführlich beschrieben wird, ist sehr einfach.

Ungeeignet für diese Behandlungsmethode sind weit vorgeschrittene Fälle, sowie solche mit schwererer Beeinträchtigung der Knochenleitung oder mit ausgesprochener Beeinträchtigung des Hörvermögens für hohe Töne.

THE purpose of the investigation was twofold. The first objective was to ascertain if, by producing an active congestion in the minute blood-vessels of the organ of hearing in cases of otosclerosis, any improvement in the hearing occurred, and thus test the correctness or incorrectness of the author's view of the ætiology of the diseases, as expressed by him in the Dalby Memorial Lecture of May 1934 (Gray: *Proc. Roy. Soc. Med.*, 1934, xxvii). The second objective, and from the human point of view the more important, was to find out if such improvement could be rendered of sufficiently long duration as to be of practical value in relieving these patients of their deafness in greater or less degree.

It should be added that the writer was encouraged to undertake this investigation by knowledge of the fact that cases of otosclerosis occurred in which striking improvement took place temporarily, under circumstances which brought, for the time being, an extra supply of blood to the organ of hearing. These were cases to which he gave the name otosclerosis paradoxica (Gray: *Journ. of Laryngol. and Otol.*, xxxviii, 141), and their occurrence offered a faint ray of hope that the condition might be produced artificially by some means or other.

For the purpose just mentioned it was first of all necessary to find some agent which, when applied locally, would produce an active congestion of the blood-vessels and at the same time be free from any irritating qualities which might cause inflammatory reaction. In this matter the writer was greatly helped by a clinical observation which he himself made when carrying out an investigation on quite another subject thirty years ago. At that time, being much annoyed by the symptoms of faintness and giddiness which frequently occurred when watery solutions of cocaine were applied to the mucous membrane of the nose, he made some experiments in order to find a more satisfactory way of applying the drug. After various substances had been tried, the difficulty was ultimately overcome by employing vaseline as the vehicle for applying the cocaine, and adding to the ointment powdered dried extract of the suprarenal glands. (Adrenaline at that time had not yet been isolated.) This ointment proved very satisfactory and the writer had no further difficulty with attacks of faintness and palpitation in his patients as a result of using cocaine. From the present point of view, however, the interest lies in a fact observed during the investigation just recorded. Among the substances which were tried in combination with cocaine, was dried extract of the thyroid gland. This substance, however, did not seem to have any effect in increasing the anæsthesia, as did the suprarenal extract. But a different and unexpected result *did* occur. The patients noticed a slight increase in nasal

obstruction which lasted for two or three weeks. On inspection of the nose the explanation of this obstruction was found in the fact that the turbinated bodies, and the mucous membrane generally, were in a condition of mild *active* congestion. That is to say, they were swollen to a moderate degree, such as is found in ordinary acute nasal catarrh, but the colour was a bright red or pink, very different from the crimson appearance of a passive congestion.

The recollection of this clinical observation made by the writer thirty years ago proved invaluable in the present investigation. It indicated, without further search, an agent which apparently fulfilled at least some of the qualities necessary for the purpose. That is to say, it produced in the mucous membrane a prolonged active congestion and at the same time caused no evident irritation. Obviously, therefore, it was natural to try the local effect of thyroid gland extract first, and, as the event ultimately proved, it was very satisfactory. In recent times, however, owing to the work of Kendall, Barger, and other biochemists, the active principle of the gland, thyroxine, has been isolated, and is now made synthetically, and this preparation is more satisfactory for practical use than the crude dried extract of the gland itself.

This explanation of the reason for employing thyroxine is necessary in order to prevent a misunderstanding. Otherwise it might have been assumed that the drug was applied for the purpose of compensating locally for a general deficiency of thyroxine in the patient's blood. Now, there is no evidence whatever that any deficiency of the natural hormone of the thyroid gland occurs in otosclerosis; and thyroxine was not selected in order to compensate for any such supposed deficiency. It was chosen solely on account of its local action as observed by the writer, and any other substance which has a similar local action would do equally well. But the writer does not know of any other such agent.

Thyroxine may be obtained from manufacturing chemists in the form of tabloids of $\frac{1}{64}$ gr. (0·001 grm.) and $\frac{1}{640}$ gr. (0·0001 grm.), the first representing the official maximum dose. The writer usually employed half the maximum dose ($\frac{1}{128}$ gr.); and although this may appear somewhat large for individuals who are not deficient in their own natural thyroid secretions, it must be pointed out that they only receive the thyroxine once weekly. In any case no evidence of hyperthyroidism occurred in any of the patients, and indeed, most of them remarked how well they felt in general health as the result of the local treatment, and several put on weight as well. In one case a curious clinical fact is to be recorded (Case V). It was that of a married woman, a nullipara, aged 25, in whom menstruation had always been very regular, and unaccompanied by any discomfort. When the treatment with thyroxine injections into the tympanic cavity was being carried out menstruation occurred every three weeks, and was accompanied by a certain amount of discomfort. Otherwise she felt remarkably well. The menstrual disturbance may have been merely a coincidence, or it may have been associated with the absorption of thyroxine, and further clinical observation on other cases will be necessary before a definite opinion can be formed in regard to the matter. At present the clinical fact falls to be recorded. When it is pointed out that the patients only receive four or, at most, six injections, and that these are spread over a period of at least four or six weeks, it appears to be very unlikely that any serious harm could come from overdosage, unless a patient was already the subject of hyperthyroidism. So much does this appear to be the case that the writer intends in future to employ doses of $\frac{1}{64}$ gr. in adults.

The method employed in the application of thyroxine to the ear consists of injecting the drug, suspended in four minims of distilled water, through the tympanic membrane into the inner middle ear by means of an ordinary well-made and smooth-working hypodermic syringe. The needle of the syringe must, of course, be a little longer than those used for ordinary hypodermic injections in order that the point

may reach the membrane and project for the distance of a millimetre or two into the middle ear. Furthermore, the needle must be bent at its proximal end in order that the line of vision be not obstructed by the barrel of the syringe or the hand of the operator. Another matter of some importance is the point of the needle. The bevel at the tip of the needle should not be long and tapering, but short and stumpy, somewhat similar to that of the needles used for intravenous injections. The calibre of the needle should be small. Needless to say, the proximal end of the needle must fit with air-tight closeness to the nozzle of the syringe.

The tabloid of thyroxine must be crushed down with a small spatula to the finest possible powder, otherwise some undissolved particle may block the needle at the critical moment when the fluid is being injected into the middle ear. The powdered tabloid, or as much of it as the operator wishes to use, is then mixed with not more than four, or at most five, minims of distilled water. If more than that amount of water is used, some is liable to escape down the Eustachian tube or back through the puncture into the meatus.

Anæsthesia of the tympanic membrane is obtained by the instillation of 15 or 20 drops of the solution introduced by the present writer for this purpose many years ago. It consists of 10 parts of cocaine hydrochlorate dissolved in 90 parts of aniline. The aniline must be freshly prepared and should be colourless or of a very faint straw tint. And here a word of caution is necessary. Aniline is a strong agent and, moreover, has a remarkable faculty of penetrating the skin. Indeed, it is this latter property which led the writer to employ it as a vehicle for cocaine for anæsthetizing the tympanic membrane. Therefore, after the drops have been in the meatus, with the patient's head resting sideways on a table, for five minutes, it is very important to dry out carefully all the aniline and cocaine solution with cotton-wool mops. If this is done thoroughly, until no trace of aniline remains in the meatus, there need be no fear of symptoms of aniline poisoning. This is a point important to remember.

Before proceeding to make the injection, a broad cork is placed between the upper and lower jaws of the patient. The object of this is to keep the mouth wide open and thus prevent the patient from swallowing after the injection is made, which would permit a part of the solution to escape down the eustachian tube. As wide a speculum as possible is then inserted into the meatus and the membrane well illuminated in the ordinary way by the forehead mirror. The point at which the puncture is made should be as nearly as possible in the middle of a line drawn horizontally backwards from the tip of the handle of the malleus to the margin of the tympanic ring. Thus, any possible injury to the long process of the incus or to the stapes is avoided, and at the same time the puncture is sufficiently above the floor of the tympanum to prevent any appreciable amount of the fluid escaping back through the puncture into the meatus.

In making the puncture it is important to remember that the plane in which the membrane lies is very oblique relative to the line of vision. Therefore, when the point of the needle is seen to be in contact with the membrane, it should be pushed backwards as well as inwards as the puncture is being made. This movement also allows the point to pass behind the bony lip of the round window and thus escape being impacted in the promontory. The fluid is then injected and a large proportion of it will lie in the space behind the round window and below the oval window. The needle is then withdrawn and the patient's head is immediately bent backwards so that he is looking up towards the ceiling. The reasons for this are to keep the fluid so far as possible bathing the region of the round window, and also to prevent it running down into the eustachian tube. The head is kept in this position for from five to ten minutes, after which time the natural position may be resumed and the cork removed from the mouth. If the procedure has been carried

out successfully, the patient usually feels the presence of a little of the fluid in the nasopharynx and may even taste it in the mouth.

The whole procedure is painless, or as nearly so as possible. A slight feeling of giddiness is frequently present immediately after the injection, but this passes off in the course of a minute or two. Except for this there is no reaction and the patient can resume his work at once. In cold weather a plug of cotton-wool should be inserted into the meatus to prevent any possibility of the tympanic membrane becoming chilled; and the patient should be instructed not to blow his nose if possible for some time after injection.

In only one case was there any inflammatory reaction to the procedure, and in that case the trouble may, with justice, be ascribed, not to the injection of thyroxine but to the fact that within a few hours after the injection the patient put into the meatus fifteen drops of radiostoleum that had been prescribed to be taken internally. There can be little doubt that the inflammation and suppuration which followed were the result of radiostoleum filtering through the puncture and were not due to the thyroxine. In proof of this is the fact that in this patient thyroxine had been injected on three previous occasions without causing any reaction. The inflammatory reaction was not very acute; the subsequent suppurative discharge dried up completely within two weeks, and the improvement produced by the previous injections of thyroxine gradually returned spontaneously.

Another contingency, which has occurred in two or three of the cases treated by the writer, is hæmorrhage within the tympanic cavity. This is due to the point of the needle having punctured some minute blood-vessel either in the tympanic membrane or on the inner wall of the tympanic cavity. It is recognized by the deep crimson, or almost black, appearance which it gives to the lower portion of the membrane, associated with the fact that a pledget of cotton-wool applied to this region does not come out stained with blood, because the membrane is outside the clot. In none of the cases in which this occurred has there been any inflammatory reaction, nor has it apparently interfered perceptibly with the beneficial effect on the hearing produced by the injection of the thyroxine. It is nevertheless, an undesirable incident, because, in the opinion of the writer, it would not be wise to repeat the injection until the clot was absorbed, for fear of the possible introduction of pyogenic organisms with resulting middle-ear inflammation. As the clot takes several weeks to disappear, the treatment must be correspondingly interrupted. It is doubtful if this hæmorrhage can always be avoided, but the chance of its occurring is greatly diminished by employing a fine needle, by taking care that the point of the needle passes behind the bony lip of the round window and is kept very steady during the whole procedure.

When the meatus is narrow the procedure is obviously rendered more difficult. In none of the cases hitherto seen by the writer was the meatus so narrow that the operation could not be carried out, but in one or two of them it very nearly came into that category. It is inevitable, however, that sooner or later, cases will come under observation in which the field of operation is so obscured by narrowness of the meatus, that it would be unwise to attempt to make the injection blindly as would be the case in such a condition. Fortunately, such cases will be uncommon, and when they do occur special measures will have to be adopted to allow of the procedure being carried out.

Although inflammatory reaction does not occur after injection of thyroxine, there is sometimes a slight degree of headache on the side upon which the operation has been performed. This passes off in the course of a day or so.

It goes without saying that careful antiseptic precautions should be taken throughout. The meatus should be well mopped-out with rectified spirit before the anæsthetizing solution is instilled. Aniline itself is a powerful antiseptic and its

faculty of penetrating deeply into the epidermis enables a thorough asepsis of the meatus and membrane to be obtained.

There is, of course, no satisfactory method of making the nose or nasopharynx really aseptic, and the most that can be done to avoid infection from this source is to be careful not to carry out the undertaking during the course of an acute nasal catarrh. Chronic nasal or nasopharyngeal catarrh apparently does not tend to cause inflammation of the middle ear after the injection is made, and in several of the cases reported below the patients were suffering from this condition, and no inflammatory reaction occurred. The injections have usually been made at weekly intervals, so that each ear gets an injection once a fortnight. In some cases, however, the intervals have been a little longer, and this does seem to affect the efficacy of the treatment. If the hearing had not improved after an ear had had two injections, the treatment was discontinued.

Although the writer has given, in the preceding pages, a detailed description of the procedure, it must not be supposed that there is any difficulty about it. On the contrary the whole undertaking is simple in the extreme, and any otologist can perform it without any special training in the technique. The points to be observed are, first, to take care that the tip of the needle does not penetrate so deeply into the middle-ear as to impinge upon the inner wall of the cavity, and second, to keep the syringe absolutely steady so that the tip of the needle does not wobble about. The piston of the syringe must run smoothly and easily in the barrel so that little pressure is required to inject the solution.

The writer carried out the treatment just described in fourteen cases, and short reports on all these cases are given below.

I.—D. S., female, aged 18 years, unmarried.

August 1, 1934: Has noticed a gradually increasing deafness in the right ear for six months and in the left ear for one year. Occasional tinnitus occurs in the left ear, but not in the right. Paracusis has not been observed. Inflation and other methods of treatment have done no good.

Right ear		Left ear
Pale	Membrane	Pale
6 in.	Watch	2 in.
− 12 sec.	Rinne	− 18 sec.
Lost below Sol $_{-1}$	Low notes	Lost below Re $_{1}$
All heard well	High notes	All heard well
2 ft.	Whisper	1 ft.

November 7, 1934: Patient thinks the hearing is getting worse.

January 21, 1935: Injection of $_{3}\frac{1}{2}$ gr. of thyroxine into left middle ear.

January 31, 1935: Patient thinks the hearing is about the same as before. Injection of $_{1}\frac{1}{2}\frac{1}{8}$ gr. of thyroxine into right middle ear.

February 14, 1935: Patient feels that the hearing in the left ear is better, and the fact is also noticed by her friends. Watch, 6 to 8 in. right, 3 in. left. Whisper, 3 ft. right, 2 ft. left. Injection of $_{1}\frac{1}{2}\frac{1}{8}$ gr. of thyroxine into right ear.

March 2, 1935: Tinnitus is now quite gone. Watch, 6 to 8 in. right ear, 4 in. left ear. Whisper, 5 ft. right ear, 2 ft. left ear.

March 12, 1935: Improvement maintained, but no further increase since last note. A blood-clot is present in the left middle ear.

April 3, 1935: Watch, 1 ft. right ear, 4 in. left ear.

II.—S. F., male, aged 29.

September 19, 1934: Has been dull of hearing for ten years, with very gradual onset. Had tinnitus in the earlier course of the deafness, but not now. Paracusis is only doubtfully present. Mother began to be deaf about the age of 60, but with this exception there is no deafness in the family. The right ear is rather the better hearing ear, but there is little difference between right and left.

Right ear		Left ear
Somewhat opaque	Membrane	Somewhat opaque
No rosy tint		No rosy tint
Perhaps a little indrawn		
Not heard by either air or bone	Watch	Not heard by either air or bone
6 to 8 in.	Whisper	6 to 9 in.
4 to 5 ft.	Conversational voice	4 ft.
− 22 sec.	Rinne	− 19 sec.
Slight loss	High notes	Slight loss but not quite so much as in right ear

October 28, 1934: Injection of $\frac{1}{120}$ gr. of thyroxine into left tympanic cavity. Some of the fluid escaped through the puncture back into the meatus. Patient felt a tickling sensation in nasopharynx a few minutes after injection.

November 10, 1934: Hearing perhaps a little better in left ear. Conv. V. 5 to 6 ft. left.

Between November 11, 1934, and January 12, 1935, two injections of thyroxine were made, and the hearing continued to improve.

January 12, 1935 to March 2, 1935: Three injections of $\frac{1}{120}$ gr. thyroxine made between these dates. Suppuration occurred in the left ear as the result of putting radiostoleum by mistake into the ear (which was ordered to be taken internally) a few hours after the injection of thyroxine had been made. The suppuration dried up within two weeks. In spite of this, the hearing, though not quite so good as noted in last entry, is very much better than it was originally and is again improving.

April 27, 1935: Watch, right ear, heard only by bone-conduction, left, 1½ in. Whisper, 1 ft. right, 3 ft. left.

III.—Mrs. B. C., aged 38.

September 27, 1934: Dullness of hearing, of gradual onset, and increasing during the last ten years. Tinnitus occurs frequently in both ears, but is not continuous. Paracusis is definitely present. There has never been any pain or discharge from the ears. There is no history of family deafness. The patient has frequently been treated by inflation of the middle ear per catheter but without any improvement. The right ear is the worse as regards hearing.

Right ear		Left ear
Possibly a little indrawn	Membrane	Possibly a little indrawn
1½ in.	Watch	3½ in.
− 25 sec.	Rinne	− 20 sec.
15 in.	Whispered voice	2 ft.

October 3, 1934: Thyroxine ($\frac{1}{120}$ gr.) was injected into right tympanic cavity. No pain after injection, but a very slight feeling of giddiness which passed off in a few minutes.

October 8, 1934: For a day after the injection the ear felt full, but there was no pain. Tinnitus began to get worse almost immediately after the injection. There was no giddiness or pain at any time. Patient's friends think she is hearing a little better, but patient herself is not sure of this. On examination a large blood-clot is seen through the membrane in the anterior part of the tympanum. Patient felt a certain amount of fullness in the left ear as well as in the right immediately after the injection. Whisper, 2½ ft. right, 3 ft. left, so that improvement appears to have occurred in both ears.

October 16, 1934: Patient is now quite sure that her hearing has improved, and her friends notice the same. The tinnitus is still present, but is less severe. No fullness in the ear. Watch, 4 in. right, 4 in. left.

October 23, 1934: Hearing still improving. Watch, 5 in. right, 4 in. left. Whisper, ca. 3 ft. right, ca. 3 ft. left. The blood-clot is still present in the tympanum, but is getting smaller. The patient is now greatly struck by the improvement in hearing, and she notices that not only does she hear voices better but other sounds also, such as knocking on the door, church bells, &c.

IV.—E. S., male, aged 42.

October 9, 1934: Has been deaf for eighteen years. Deafness was of gradual onset, and began first in left ear. Never any pain or discharge from ear. Has been inflated frequently without benefit. No known family history of deafness. Tinnitus of a hissing character is always present. Paracusis willisii definitely present, but not very strikingly so.

Right ear		Left ear
1½ in.	Watch	1 in.
4 ft.	Whisper	2 to 2½ ft.
− 6 sec.	Rinne	− 10 to 12 sec.
	Weber, to left	
Lost below Re_1	Low notes	Lost below Ut_2
Hardly any loss	High notes	Lost rather more than in right
Indrawn and rather opaque	Membrane	Indrawn and opaque

October 15, 1934: Injection of $\frac{1}{120}$ gr. of thyroxine into left tympanic cavity.

October 22, 1934: No pain after the injection. Patient has not noticed any difference either in the hearing or the tinnitus since the injection. Blood-clot within tympanum.

November 12, 1934: No difference in either the hearing or the tinnitus. Blood-clot still present in the tympanum.

January 28, 1934: Hearing and tinnitus remain the same as before. No further treatment advised.

V.—Mrs. K., aged 25.

October 16, 1934: Had been gradually getting dull of hearing during the last five years. No pain or discharge from ear at any time. Ears had been frequently inflated by catheter and the air passed freely up to tympanum, but produced no improvement. Paracusis willisii strikingly present. Suffers from head noises which are worse when tired. Was operated on for some nasal trouble some years ago.

Right ear		Left ear
Normal	Membrane	Normal
2½ in.	Watch	2 in.
2 ft.	Whisper	1½ ft.
− 15 sec.	Rinne	− 18 sec.
Equal in both ears	Weber	Equal in both ears
Lost below fa_1	Low notes	Lost below sol_1
Very well heard	High notes	Very well heard

October 30, 1934: Injection of $\frac{1}{120}$ gr. of thyroxine into left ear. Slight feeling of giddiness for a minute or two after injection, and slight feeling of dullness and fullness in the ear, and a sensation of tickling in the throat.

November 6, 1934: No pain in the ear after the injection or since, but very slight headache on the left side for a day or two. Patient and her friends say she is hearing better. Watch, right ear 2½ in., left, 2½ to 3 in. Whisper, 3 ft. left ear. Tinnitus about the same as before. No blood-clot inside the tympanum.

December 12, 1934: Hearing distinctly better. Patient is now able to hear the wireless and such sounds as shutting of doors which formerly she could not hear.

December 14, 1934: Improvement still increasing in left ear. Watch, 4 in. right, 2½ in. left. Patient notices that wax is now present in the ears, which formerly were dry. Injection of $\frac{1}{120}$ gr. thyroxine into left middle ear.

January 14, 1935: Whisper, 3½ ft. right, 4 ft. left. Injection of $\frac{1}{120}$ gr. thyroxine into right middle ear.

February 11, 1935: Watch, right ear 5 in., left 4 in. Whisper, right ear 3 ft., left 5 ft. The tinnitus is now very much diminished and hardly disturbs the patient at all. Injection of $\frac{1}{240}$ gr. thyroxine into right ear.

March 12, 1935: Improvement maintained. Paracusis is not noticed and the tinnitus is almost gone. The patient is feeling very well and has put on weight. It is interesting to observe that menstruation, which formerly was very regular every four weeks and unaccompanied by any discomfort, now occurs every three weeks and is attended with a little discomfort.

April 15, 1935: Improvement still maintained. Tinnitus remains absent. Watch, 6 in. right, 4 in. left. Whisper, 4 ft. right, 3½ ft. left. Low notes are now better heard: above si_{-1} in right ear, and fa_1 in left ear. Wax is still being secreted in both ears.

VI.—F. W. L., male, aged 45.

October 17, 1934: Has been deaf in the left ear since boyhood. Began to be deaf in the right ear about five years ago, and the deafness was accompanied by tinnitus. The latter is severe and is usually worse in the right ear, but occasionally worse in left. There is no pain.

The tinnitus diminished under treatment with bromide, but the hearing did not improve. Paracusis is present. There is no deafness in the family. Inflation by catheter makes both hearing and tinnitus worse.

Right ear		Left ear
Opaque and indrawn	Membrane	Opaque and indrawn and an atrophic patch in ant. inf. quad.
Not heard by either air or bone	Watch	Not heard by either air or bone
Not heard at all	Whisper V	Not heard at all
1½ to 2 ft.	Con. V	6 in.
− 12 sec. ca.	Rinne	− 10 sec. ca.
Lost below mi_1	Low notes	Lost below $a1_2$
Much loss above Mdh. 8·0 pft. 5·5 on Galton's whistle	High notes	Much loss Mdh. 8·0 pft. 7·0 on Galton's whistle
20 to 25 sec.	Absolute bone conduction	20 sec.

October 31, 1934 to March 12, 1935: Three injections of $\frac{1}{125}$ gr. thyroxine made at long intervals. On the whole, the condition was not improved, with regard either to the hearing or to the tinnitus. It is interesting to note, however, that occasionally the hearing would suddenly improve in a striking way, and at the same time the tinnitus almost disappeared. These intervals, however, only lasted for a few hours, or a day at most, and were not very frequent. No further treatment, therefore, was advised. The case, in spite of the failure to give any lasting relief, is interesting on account of the intervals during which improvement occurred. It resembles in this respect the cases of otosclerosis paradoxica described by the writer. (Gray, *loc. cit.*)

VII.—V. W., female, aged 31.

November 14, 1934: Deafness began at the age of 18 years and tinnitus at 20. The onset was gradual and has steadily become worse. There has never been any pain or discharge. The general health is very good. Paracusis was present until a year ago, when an operation was performed upon the nose. Since then the paracusis has not been noticed, and the tinnitus has become worse.

Right ear		Left ear
Heard by bone only	Watch	Not heard by either air or bone
Rosy tint over promontory	Membrane	Rosy tint over promontory
4 in.	Whisper	4 in.
− 12 sec.	Rinne	− 15 sec.
Lost below $fa_2^{\sharp\sharp}$	Low notes	Lost below si_2
Great loss	High notes	Very great loss

December 5, 1934: Injection of $\frac{1}{125}$ gr. thyroxine into right middle ear.

December 11, 1934: Hearing no better. Tinnitus perhaps slightly less. Injection of $\frac{1}{125}$ gr. thyroxine in right middle ear.

January 18, 1935: Hearing exactly the same as before treatment, and the same is true of the tinnitus. No further treatment advised.

VIII.—D. M., male, aged 30.

November 22, 1934: Deafness of very gradual onset began twelve years ago. Has had considerable amount of catarrh in nose and throat. Tinnitus not present. Paracusis not present—in fact, patient hears worse in a noise. Mother began to be deaf at the age of 30 or before. Has one sister deaf, but she suffers from otorrhœa. Has been inflated frequently, but the improvement lasts only a few minutes.

Right ear		Left ear
Normal or perhaps a little indrawn	Membrane	Normal or perhaps a little indrawn
1½ in.	Watch	Heard on contact only
9 in. to 1 ft.	Whisper	6 to 9 in.
22 sec.	Absolute bone conduction	20 to 22 sec.
− 12 to 15 sec.	Rinne	− 12 sec.
Badly affected. Lost below sol_2	Low notes	Badly affected. Lost below sol_2
Well heard. None lost of Galton's whistle	High notes	Well heard. All notes of Galton's whistle heard

November 26, 1934 : Injection of $\frac{1}{128}$ gr. thyroxine into left tympanum.

December 6, 1934 : Patient thinks he hears better and friends think so also. Watch 1 in. left. Whisper 18 in. left. Watch, $1\frac{1}{2}$ in. right, and whisper, 1 ft. to $1\frac{1}{2}$ ft. right. There is thus improvement for the whisper in the right ear as well as in the left. The improvement began on the second, third or fourth day, but patient is not quite sure which.

December 8, 1934 : Injection of $\frac{1}{128}$ gr. of thyroxine into right ear. The improvement in the left ear is still present, but is stationary.

January 12 to March 12, 1935 : Two injections made into each ear during this period. Great improvement in the hearing has occurred. Wax, which was formerly absent from the meatus, is now being secreted freely. Watch, 3 in. right, $1\frac{1}{2}$ in. left. Whisper, 18 in. right, 10 in. left.

IX.—B. S., female, aged 25, unmarried.

November 27, 1934 : Dullness of hearing first noticed in both ears, about three years ago. The onset was gradual. Paracusis is present, as also is distressing tinnitus. There is no family history of deafness. Inflation of the middle ear has been tried several times, but without any benefit.

Right ear		Left ear
Normal	Membrane	Normal
Not heard by air or bone	Watch	Not heard by air or bone
6 in.	Whisper	7 to 9 in.
− 15 sec.	Rinne	− 10 sec.
15 to 18 sec.	Absolute bone conduction	20 sec.
Lost below fa_1	Low notes	Lost below re_1
Very slight loss	High notes	Very slight loss

December 6, 1934 : Injection of $\frac{1}{128}$ gr. thyroxine into right ear.

December 13, 1934 : Had slight pain and giddiness on the day of the injection, but this had disappeared the following day. Patient noticed improvement in the hearing on the fourth day after injection. Watch, right ear $\frac{1}{2}$ in. distance. Whisper, 8 in. Patient now hears from her house the traffic in the street which she could not do previously.

December 18, 1934 : The hearing is still improving and the tinnitus is much less. Her friends notice the great improvement in her hearing. Injected $\frac{1}{128}$ gr. thyroxine into left ear.

January 10, 1935 : Improvement in hearing maintained and the tinnitus has almost entirely disappeared. Whisper, 9 in. right, 9 in. left.

January 15, 1935 : Injection of $\frac{1}{128}$ gr. thyroxine into right ear.

March 12, 1935 : Three injections have been made since the last note. Hearing is now greatly improved. Watch, 2 in. right, contact left. Tinnitus is almost gone.

X.—Miss T. B., aged 15.

December 5, 1934 : Has always been a little dull of hearing, but the dullness has become worse during the last year. No pain and no giddiness. There is occasional tinnitus and paracusis willisii is definitely present. There is one second cousin deaf, but otherwise no deafness is known in the family history. Patient has had the ears inflated frequently without benefit. The left ear is rather the worse of the two.

Right ear		Left ear
Rosy-pink tint on promontory	Membrane	Normal
− 9 sec.	Rinne	− 17 sec.
20 sec.	Absolute bone conduction	25 sec.
Lost below re_1	Low notes	Lost below sol_1
None on Galton's whistle lost	High notes	None on Galton's whistle lost
Heard only on contact	Watch	Heard only on contact
18 in.	Whisper	1 ft.

December 10, 1934 : Injection of $\frac{1}{128}$ gr. of thyroxine into *left* middle ear.

December 15, 1934 : Some improvement in hearing. Watch, 1 in. from left ear ; contact only in right. Injection of $\frac{1}{128}$ gr. of thyroxine into right middle ear.

January 9 to March 5, 1935 : Five injections of $\frac{1}{128}$ gr. thyroxine made. Hearing is now much improved. Watch, 1 in. right, $1\frac{1}{2}$ in. left. Whisper, 3 ft. right, 2 ft. left. Patient notices that she hears the wireless much better.

XI.—Mrs. W., aged 31.

December 11, 1934: Deafness of fifteen years' duration. The onset was gradual, and at no time has there been any pain or discharge. Paracusis is definitely present but there is no tinnitus. Inflation of the middle ear has frequently been carried out, but without any lasting benefit. The hearing is worse when patient is tired. There is no deafness recorded in the family history. The watch is heard at a distance of 2½ in. in the right ear, and 1 in. in the left.

January 5, 1935: Injection of $\frac{1}{128}$ gr. of thyroxine into left middle ear. The patient, who is of a nervous temperament, fainted immediately after the injection. She admitted that this was due to nervousness and not to the pain, which was insignificant.

February 14, 1935: No improvement in the hearing. It was decided not to continue treatment until the patient is stronger.

XII.—S. S., male, aged 13 years.

January 14, 1935: Patient has been getting deaf very gradually for the last two years in the right ear, and recently the left ear appears to be becoming affected. Neither tinnitus nor paracusis has been noticed by the patient. There is no deafness in the family.

Right ear		Left ear
Slight rosy tint over promontory	Membrane	Slight rosy tint over promontory
6 in. ca.	Watch	9 in. ca.
+ 10 sec. ca.	Rinne	+ 12 sec. ca.
Fork heard better in right	Weber	Fork heard worse in left
Lost below si_{-1}	Low notes	Lost below fa_{-1}
Well heard	High notes	Well heard
27 sec.	Absolute bone conduction	35 sec. ca.
2 ft. ca.	Whisper	2 yd. ca.

Injection of $\frac{1}{5}\frac{1}{0}$ of thyroxine in right ear.

January 18, 1935: Hearing remains the same as last note so far as the patient is aware.

March 6, 1935: Hearing remains the same so far as the patient is aware, but on examination he appears to hear the whisper now at a distance of 4 ft. from the right ear. Injection of $\frac{1}{5}\frac{1}{0}$ gr. thyroxine into left ear.

March 18, 1935: Letter from patient in which he says that he "thinks he hears a little better, but is not sure."

No further treatment advised.

XIII.—G. M., male, aged 21.

January 15, 1935: Deafness began five years ago with gradual onset. Paracusis is present. Tinnitus was formerly present, but has now disappeared. There is no family history of deafness.

Right ear		Left ear
Normal	Membrane	Normal
2 to 3 in.	Watch	2 to 3 in.
15 in.	Whisper	12 in.
− 10 sec.	Rinne	− 12 sec.

The Eustachian tubes are clear. Inflation per catheter produces no improvement.

February 2, 1935: Injection of $\frac{1}{5}\frac{1}{0}$ gr. of thyroxine into the left middle ear.

February 13, 1935: No improvement of the hearing has occurred since last note.

February 20, 1935: No improvement. The hearing is the same as before treatment. No further treatment advised.

XIV.—F. O., male, aged 53.

January 17, 1935: Has been deaf in the right ear since childhood, and in the left since about the age of 21. There is no known record of deafness in the family. Paracusis is present, but tinnitus is not.

Right ear		Left ear
Old dry perforation scarred over behind handle of hammer	Membrane	Normal
1 ft.	Conv. voice	4 ft.
Not heard	Whisper	2 in.
Much diminished	Bone conduction	Diminished

Blood-vessels along the handle of the hammer are not visible in either membrane.

Injection of $\frac{1}{125}$ gr. of thyroxine into left middle ear.

January 21, 1935 : Repeated injection of $\frac{1}{125}$ gr. of thyroxine into left middle ear. Patient has occasionally had short intervals of improvement in the hearing lasting for an hour or two, but, except for these intervals, the hearing remains about the same.

January 28, 1935 : After the last injection fairly severe tinnitus occurred. The noise was of a "rushing" character and gradually passed off after a day or two.

February 5, 1935 : Injected $\frac{1}{125}$ gr. thyroxine into left ear.

February 14, 1935 : A little hæmorrhage into the left meatus occurred after the last injection. As the improvement in hearing has only been intermittent as a result of the injections, it was decided not to continue treatment at present. This case is somewhat similar to Case VI. There were occasions when the hearing improved very much for a few hours. It therefore resembles the condition described by the writer as otosclerosis paradoxica.

Of the fourteen cases above recorded, the hearing has noticeably improved in seven cases, and in the remaining seven cases no improvement has occurred. It is important to observe that in those cases in which the deafness was accompanied by tinnitus, the latter symptom diminished or disappeared along with the improvement in regard to the deafness (Cases I, III, V and IX).

Paracusis was definitely present in four of the cases in which the hearing improved. This fact is of practical importance, because that symptom is so well recognized by otologists as indicating a bad prognosis and little hope of any benefit from treatment. But in regard to the method of treatment described in this paper, this indication does not hold true, and those who wish to give the treatment a trial need not consider paracusis an unfavourable symptom when selecting the cases.

The return to functional activity of the ceruminous glands noted in Cases V and VIII, is a very interesting clinical observation. The diminution of wax, with consequent dryness of the meatus, is usually, though perhaps not always, observed in otosclerosis ; and when present is a characteristic feature of the disease. The fact of its return, therefore, is objective and conclusive evidence of the effect of the treatment on at least one portion of the organ of hearing. And it is difficult to see how the change could occur in any other way than by the return of a normal blood supply to the ceruminous glands.

An interesting feature of the cases which improved is the period of time which elapsed between the injection of the thyroxine and the first observation which the patient made of the increase in the hearing-power. This period is usually of between four and eight days' duration. It is, of course, well known to pharmacologists that when thyroxine is administered by the mouth or injected into a vein, the drug does not begin to exert its effects until twenty-four hours have elapsed. After that time the effects gradually increase in intensity and reach the maximum at about the end of a week. The effects die away very slowly. This physiological peculiarity in the delayed action of the thyroxine when acting generally in the body is, therefore, in full agreement with the delayed action when applied locally, as in this investigation.

The age of the patient is a factor of considerable importance. The best results occurred in patients whose ages were between 18 and 30 or 35, although one very good result was obtained in a woman of 38 (Case III). It is interesting to note that the two patients in whose cases only intermittent improvement occurred were aged

45 and 53 respectively (Cases VI and XIV). But even among young adults, two or three did not respond to treatment.

Another interesting fact which this research has revealed is recorded in Cases III and VIII. It will be observed that in those cases, when improvement occurred in the ear operated upon, improvement was also found in the opposite ear into which no injection had been made. When these patients said they were sure they were hearing better in the ear which had not been treated as well as in the ear which had, the writer was at first inclined to attribute it to imagination. But on testing the hearing carefully, it was found that the hearing in the unoperated ear was definitely improved. Furthermore, in one of these cases a sense of fullness occurred in the ear operated upon, for a day or so before the improvement was noticed, and a similar fullness was felt in the unoperated ear. On examining the literature of the subject the writer could find no reference to a similar phenomenon in recent times. But in his "Lehrbuch der Ohrenheilkunde" published in 1901, the late Professor Urbantschitsch of Vienna described a very similar condition. He observed that in some cases of otosclerosis—or dry catarrh of the middle ear as it was then called—the passage of the Eustachian bougie produced improvement in the hearing not only of the ear treated but of the opposite ear also. He considered that this was due to a reflex passing from one ear to the other, and termed it a crossed reflex. Little was known at that time of the functional vasomotor responses, and Urbantschitsch makes no reference to the nature of the reflex. In the light of the cases recorded in the present paper there can be little doubt that Urbantschitsch was correct in the observation of the facts. The subject, however, apparently did not arouse much interest in otological circles, probably because the cases in which the phenomenon was demonstrable were very few, and the condition itself was very transient.

Turning now to the other purpose for which this investigation was undertaken, that is, to provide a test for the writer's view of the ætiology of otosclerosis, only a few words are necessary. The improvement in hearing which resulted from producing an active congestion of the parts provides such strong evidence in favour of that view that one may almost be justified in now considering it rather as an established fact than as a hypothesis. The fact that many cases do not respond to the treatment does not appear to the writer to invalidate the hypothesis. The structural changes in the bony capsule of the labyrinth in the region of the oval window, and also those in the cochlear nerve, which result from the loss of the vasomotor response, may well have reached a stage at which repair is impossible. Furthermore, the vasomotor nerves themselves in these cases may have degenerated so far that the thyroxine fails to render them again functionally active.

For those who wish to try the method of treatment described in this paper, a few hints as to the selection of suitable cases may be helpful. It is not wise, for the present purpose, to attempt to distinguish cases of otosclerosis from the so-called chronic dry middle-ear catarrh—if such a condition has any real pathological existence. When there is a noticeable loss of hearing for the lower notes, with retention for the high ones, associated with a negative Rinne, and with no serious diminution of absolute bone-conduction, along with absence, or only slight improvement, of the hearing on inflation of the middle ear, then the treatment by thyroxine injection may be tried. Cases in which the absolute bone-conduction is seriously diminished, even when the Rinne test is negative, are not likely to respond to treatment, and the same is true when there is any very noticeable loss of the hearing for high notes. The appearance of the tympanic membrane gives little help in the selection of suitable cases, and the writer has had good results when the membrane was quite normal in appearance as well as when it was thickened and opaque. It will naturally be understood that when the deafness has become extreme, no

response to the treatment need be expected, for in these cases the structural changes both in the region of the oval window and in the nerve-elements of the organ of hearing have reached such an advanced stage that their capacity for functioning cannot be much affected by increased blood supply.

Another point which should be emphasized is in regard to the number of cases employed for investigation. Conclusions must not be drawn from the results obtained in one or two cases. The first two or three cases might all happen to fall into the category of successful responses to treatment or into that of failures, and undue optimism or pessimism, respectively, be established in the investigator's mind. When the writer began this research the first two cases happened to be highly successful, but the optimism thus aroused was sobered by the following two or three cases which did not respond to treatment. It is necessary, therefore, to try the treatment on a fair number of cases before forming a judgment on the matter.

It is at present impossible to say how long the improvement will continue without treatment being renewed. In some of the cases reported the improvement has lasted several weeks and, at present, shows no sign of diminishing, and it is possible that it may be permanent. But in all probability two or three injections will have to be made throughout the year, because we know from the natural history of the disease that the deafness tends to progress slowly. It must be expected, therefore, that any treatment, however successful, would have to be renewed at intervals.

Summary.—A large proportion (about 50%) of cases of otosclerosis and so-called dry middle-ear catarrh can be greatly improved in regard to both hearing and tinnitus by the intratympanic injection of thyroxine. Cases in which the disease is in its latest stages, however, do not respond to the treatment. The presence of paracusis willisii is no contra-indication to treatment. The method of treatment is simple and can be carried out without difficulty by any otologist. It is practically painless or altogether so, and does not interfere with the patient's daily activities.

The rationale of the treatment depends upon the writer's view that otosclerosis is the result of a diminished blood-supply to the organ of hearing, consequent upon a gradual failure of the vasomotor responses. The action of thyroxine applied locally is to produce an active congestion without inflammatory reaction, and continuing for a long period of time.

It is not yet possible to say how often the treatment may have to be repeated. The improvement, when it occurs, lasts in some cases for several weeks, but sooner or later the effects must be expected to pass off. The present paper is of the nature of a preliminary communication, and the cases shown to-day will again be reported upon next session. In the meantime the writer hopes that others will investigate the matter and let the results of their experience be known.

Discussion.—The PRESIDENT said that otosclerosis had been the greatest bugbear of the specialty. He had been struck by the fact that in the drums of the patients exhibited there were no signs of inflammation. The treatment should be used extensively in these cases.

Mr. ALEXANDER TWEEDIE said he would like to have Dr. Gray's opinion as to the way in which the thyroxine acted. Did it depend for its action on actually reaching the auditory nerve? Would it be convenient for Dr. Gray to express the hearing values in terms of cycles or double vibrations.

Mr. J. F. O'MALLEY said that twenty years ago he had conceived the idea that in otosclerosis there was a fixation of the stapes, and that the changes found were related to those in rheumatoid arthritis. Acting on that idea he had tried treatment by local applications of heat. He had made an asbestos-lined box, designed to include the whole mastoid and ear, the

remainder of the head being shut off from the heating apparatus. He had tried this in twenty cases extending over a year. The idea was not far removed from that of Dr. Gray's, as the local heating caused hyperæmia, just as injection of thyroxine did. Associated with this hyperæmia was a vasomotor reaction, which, no doubt, influenced function. When localized action was produced anywhere in the body there was a corresponding increase in vasomotor activity for the time being. The line of treatment which Dr. Gray had adopted was an exceedingly interesting sequence to the conclusions at which he had arrived as to the underlying deficiency in cases of otosclerosis. It provided otologists with a new hope.

Dr. GEORGE CATHCART said that Dr. Gray had arrived at the same conclusions as Zünd-Burguet had arrived at more than twenty years ago. Zünd-Burguet believed that it was essential to obtain local hyperæmia, and he invented the electrophonoide method[1] which appeared to give the same results as Dr. Gray's thyroxine injections. The hyperæmia of the ear (presumably of the whole internal ear) could easily be seen by inspecting the drum; again the secretion of wax was restored, and in 70% of the cases the tinnitus ceased. The tinnitus in two cases had ceased completely and permanently after the second treatment. The chief difference in the two methods of treatment appeared to be that the Zünd-Burguet method took a longer time to carry out; a week must elapse before one could tell whether improvement was likely and another week before improvement of a more or less permanent nature could be expected.

The results of Dr. Gray's treatment did not compare favourably with those obtainable from the Zünd-Burguet method. Dr. Gray did not take into account the voice. He only mentioned the whisper and seemed to imply that if hearing for the whisper improved, hearing for the voice improved *pari passu*, but that had not been his (Dr. Cathcart's) experience. Perhaps Dr. Gray's method of whispering was different from his. He (Dr. Cathcart) used the method described in his book which was one of constant strength. This was obtained by taking a breath and forcing it out again, using only the residual air for the whisper. Not one of Dr. Gray's patients shown to-day could hear that kind of whisper, and therefore he (Dr. Cathcart) had no means of judging if improvement had been produced. Case VI was an exceptionally good lip-reader, and with his eyes shut he could not hear his (Dr. Cathcart's) ordinary conversational voice at a distance of 4 ft., and yet he could hear Dr. Gray's whisper at 18 in. Cases III, IV and V stated that they could not hear ordinary conversation across the dinner table, therefore the results could not be regarded as particularly good. It would be interesting to know if a combination of the two methods would bring about a better result, and Dr. Gray had kindly promised to allow him (the speaker) to try the Zünd-Burguet method on cases which did not respond to his (Dr. Gray's) method. It would be valuable to ascertain how long the results of Dr. Gray's method remained good.

Mr. F. C. ORMEROD wished to ask whether the use of distilled water in itself produced any effect in this procedure. He thought it must produce some osmotic changes. Did distilled water assist in the hyperæmia, or would more hyperæmia follow if he used normal saline as the solvent of the thyroxine?

Mr. T. B. JOBSON asked whether Dr. Gray considered it necessary to adopt special methods of sterilizing the external auditory meatus before applying the injection.

Mr. MILLS asked whether injection of distilled water alone had any effect on controls.

Dr. GRAY (in reply) said that the effect of the injection was a dilatation of the blood-vessels throughout the organ; it was not probable that it acted by any direct effect on the cochlear nerve. If there were a proper strength and a proper osmotic tension it might then pass through the membrane of the round window; but he doubted whether, as used in the cases shown, it went through that membrane.

Local treatment by heat produced exactly the effect which was desired, because it caused dilatation of the blood-vessels, but it was difficult to produce heat in the ear, and, moreover, the effect would not last very long. One of his patients had said, three or four days after the injection, that his ear began to feel "warm inside."

He did not know how the improvement with regard to the tinnitus was to be explained by the treatment, except on the lines of general improvement in the hearing. Case V was

[1] "The treatment of chronic deafness by the electrophonoide method of Zünd-Burguet." Oxford Medical Press, 2nd edition, 1931.

an instance of striking improvement in this respect. The patient had previously been having a severe buzzing in the ears, and that had now almost gone ; it had diminished also in Cases I and III.

He had never seen any very satisfactory results from the Zünd-Burguet method of treatment. As to hearing whispers, all whispers were different; one could only estimate the intensity of one's own whisper; the watch and the audiometer constituted better standards. All the patients seemed to be pleased with the result, and that was the best test. All tests which involved the attention of a patient introduced the possibility of fallacy. It was a striking tribute to the success of the treatment that knocks and rings at the door, church bells &c., previously unheard, were now heard again.

With regard to the use of distilled water because of its effect on osmotic pressure, he was unable to answer the question. If distilled water produced any effect on the hearing it was difficult to see how that effect could last for several weeks.

Before injecting the thyroxine he mopped the meatus out with spirits. It must be remembered that aniline itself was a powerful antiseptic, and was able to penetrate the skin.

He had no reason to suppose that distilled water alone would improve the hearing, whereas he thought that thyroxine would, because of his former experience with it as applied to the nose. The injection of distilled water could not be expected to produce improved hearing four days later and to continue that improvement for weeks, and also cause a freer secretion of wax in the external auditory meatus.

Section of Medicine

President—Sir FARQUHAR BUZZARD, Bart., K.C.V.O., M.D.

[*May* 28, 1935]

The Use of Sanocrysin in the Treatment of Pulmonary Tuberculosis

By G. GREGORY KAYNE, M.D., M.R.C.P.

MØLLGAARD brought forward the chemical and experimental work relating to sanocrysin in 1924 and he was able at the same time to give Secher's results of the first clinical trials in man. Investigations were initiated without delay and carried on with enthusiasm in many parts of the world. Ten years should, in these circumstances, be sufficient to demonstrate the efficacy of a method of treatment in a disease as common as pulmonary tuberculosis. Unfortunately no unanimity of opinion has been reached. Those who see a tuberculous basis in diseases so widely apart as rheumatoid arthritis and dementia præcox, would use it in almost all illness to which human nature is heir. Others, even in pulmonary tuberculosis, consider it more advantageous to place the gold in the patient's pockets rather than in his veins. And between these two extremes many shades of opinion or differences of practice exist, as regards indications, mode of application, and results obtained. My remarks to-day are not based on experience gained in treating patients myself, but on observations made as the result of personal contact with several European workers. After sketching the outlines of past experimental work, I propose to review briefly the guiding principles of sanocrysin therapy in the centres I visited, and in the light of these, attempt to present conclusions as to indications and mode of application.

Experimental Work

It is generally agreed that sanocrysin has no marked effect on tubercle bacilli *in vitro*. Møllgaard claimed, however, that it has a direct bactericidal effect in the animal body. He adduced at least three arguments in support of his opinion. He states [8] that "a quarter, and in some cases one-tenth, of the dose which is without effect on the healthy animal, produces the most severe reactions in the tuberculous organism . . ." these reactions presumably being due to liberation of toxins following destruction of the bacilli, and similar to those following the injection of large doses of tuberculin. Histological examination of the affected organs of

treated animals, dying after severe reactions, showed morphological forms suggesting such disintegration. And, finally, the beneficial effect in regard to reactions following the use of a serum prepared by immunizing healthy animals with defatted formalin-treated tubercle bacilli seemed to favour his hypothesis. It was remarkable, however, that the injection of the gold salt at the same time as the bacilli did *not* prevent the development of tuberculous lesions (Madsen and Mørch [7]). In addition, the appreciation that the metal itself might play a rôle in producing reactions, their diminished frequency with smaller doses, and the varying results obtained with the serum, led to rejection of the theory of a direct bactericidal action and to the abandonment of the use of serum. Those admitting the beneficial effect of sanocrysin—and as will be seen below, experimental evidence, in addition to Møllgaard's, exists in support of it—invoke the possibility of sanocrysin acting as an aid or stimulant to the natural tissue-defences. Møllgaard [10] himself, in 1928, questions how sanocrysin acts and points to the unexplained mechanism of chemotherapy in general.

In 1925, O. Bang [2] carried out experiments in calves but could not confirm Møllgaard's curative findings. In spite of the latter's criticism [9] of certain details in Bang's work, Bang maintained [3] that Møllgaard's results were due to the varying resistance of animals to abnormal (attenuated) tubercle bacilli, and that the animals used for controls might already have been infected and therefore be more resistant. Madsen and Mørch [6], in 1926, showed that in rabbits, when slightly virulent bacilli were used, all the animals had reactions after small doses of sanocrysin, and the serum proved no protection, but the gold was curative. After infection with highly virulent bacilli, there were no reactions with sanocrysin; serum was therefore unnecessary, and to obtain curative results large doses of the gold salt were needed. Repeating their experiments in collaboration with O. Bang in 1928, these authors [7] could not, however, again obtain the positive results in rabbits. K. A. Jensen [5] failed to obtain definite results and could not, like Møllgaard, even produce in the rabbits the chronic predominantly pulmonary lesions. In England, Lyle Cummins [4], in 1926, concluded that sanocrysin used in appropriate doses and at an early stage in the disease had a markedly favourable action upon the course of experimental tuberculosis in the rabbit, and that the favourable effects varied inversely with the virulence of the infecting bacillus and the size of the infecting dose. Finally, more recently, Atkin (1931) [1], working with dead bacilli injected intravenously in rabbits, found that repeated injections of sanocrysin protected them from the lethal action of an intravenous injection of old tuberculin about one month later, while control animals succumbed. He states that his experiments prove that sanocrysin exerts an inhibitory effect on tuberculous lesions, apart from any bactericidal action it may have on the living tubercle bacillus.

It will be seen that there exists no clear experimental basis for the use of sanocrysin in pulmonary tuberculosis and that further work in this connexion is to be encouraged. Nevertheless, in view of the benefit derived from other remedies used empirically at first, complete rejection of its use does not appear justified. In fairness to Møllgaard and considering the many types of cases in which the gold salt has been administered, the following statement [8] from his paper in 1925 should be quoted: "It may therefore be expected that the best effect of the sanocrysin serum treatment in the human subject will be obtained in cases of the exudative pneumonic type. . . . As, however, our present treatment, inclusive of artificial pneumothorax, fails to give definite results in very many of these cases, the attempt to found a chemotherapy on sanocrysin would not have been in vain, if it should be limited to such cases."

During the last few years Møllgaard has concentrated on the bacteriology of tuberculosis and has not carried out any further experimental work with sanocrysin. His views on indication and mode of action are to-day identical with those indicated above.

Sanocrysin Therapy in Denmark.

In Denmark, Knud Secher's work must be considered first. In view of the critical remarks which follow, it should be pointed out that even an unbiassed perusal of his publications and a few weeks' personal contact may be insufficient fairly to appraise ten years' work. He is a general physician in a general hospital, whose patients constitute mainly observation cases, which, after a short stay, invariably pass on to a sanatorium. Although many of the patients are traced by Secher afterwards, it is clear that these circumstances do not favour a just appreciation of the part played by sanocrysin remotely, or even immediately, in view of the associated rest. Moreover, in his results published in 1932, 114 patients are stated [12] to have been rendered symptomless, but of these no less than 80 were classified before treatment as early or moderately severe cases *without tubercle bacilli*. Secher believes that sanocrysin causes a liberation of toxins which accounts for all the reactions that follow. He therefore bases his initial dosage on the assumption that in "open cases" the toxins can be excreted by the air-passages and therefore larger doses are permissible, while in "closed cases" smaller doses are indicated because the toxins having no outlet pass into the blood-stream. For the same reason smaller dosage is advisable in extensive than in localized lesions, in recent than in old-standing cases. His indications are wide: advanced disease, tuberculosis of other organs (especially of the intestine), but not of the larynx, being almost the only contra-indications. He even advises its use in old fibroid cases and, in addition, employs it frequently in pleurisy. The difficulty of deciding the presence of an associated pulmonary lesion and the greatly varying statistics published as to the ultimate prognosis of pleural effusions do not appear to justify Secher's enthusiasm in this connexion [13]. His initial dosage still remains the highest administered at present, for he argues, on the basis of his conception of the cause of reactions, that it is doubtful whether they should be avoided, and in fact states [12]: "On the basis of the experiments I made I believe that the reaction following treatment greatly activates the cure." He begins with 0·25, 0·35, or 0·5 grm., rising to a dose of about 1 grm., but rarely reaching a total of more than 5 or 6 grm. This fact in the light of his statement[1] tends to suggest that the beneficial results obtained by Secher are due to a form of "shock-therapy" rather than to any specific effect of the gold. This is supported by the finding of congestive areas around tuberculous lesions in the fatal cases which occurred in the days when even larger doses were used. I must, however, also admit that I was impressed by seeing several patients who had had pyrexial reactions associated with albuminuria, or erythema, on more than one occasion, in whom subsequent injections of even larger doses produced no reaction at all. The greater frequency of erythemas in the early stage of sanocrysin treatment, also noted by Sayé and others, argues against the gold as their cause. It may also be pertinent to quote here Professor Knud Faber's statement to me that while he could in no way be dogmatic as to the value of sanocrysin, he felt convinced that in the early days of large dosage remarkable curative results, not seen now, were occasionally obtained.

Gravesen's use of sanocrysin at Vejlefjord Sanatorium is of a different character. He considers that the ideal indication is the early exudative lesion, whether occurring

[1] "I myself do not wish to apply very feeble doses of a few cg. progressively, as I believe that one contributes in this way to increase the metallic store which forms in the organism before coming to doses which have really a therapeutic effect."

by itself or in association with older processes—when, however, a palliative effect only can be expected. The type of material he deals with tends to make him use sanocrysin as a valuable aid in collapse-therapy—to clear one side before attempting surgical intervention on the opposite older lesion, or to treat a contralateral extension of disease after artificial pneumothorax or thoracoplasty. The presence of cavitation, even in a unilateral exudative process, compels the institution of an artificial pneumothorax, although sanocrysin may be given in addition. Old-standing disease with fibrosis or cavitation should be considered a contra-indication. His dosage is moderate. Beginning with 0·1 grm. the dose is gradually increased, a one-day interval being allowed for each 0·1 grm., in the last dose given—unless reactions occur—to a final dose of 0·75 grm., or occasionally to 1 grm. About 2·5 grm. are administered during the first month and the total course of about 5 grm. is repeated afterwards. Reactions are avoided as far as possible, but in a series of 500 cases two fatalities have occurred; one patient whose prognosis was already unfavourable died from acute nephritis, and the other succumbed to purpura two weeks after returning home.

Two other workers in Copenhagen who have used sanocrysin extensively—C. H. Würtzen and Permin—did not appear to have very definite convictions as to its efficacy. Würtzen employs it less than formerly, and Permin, who favours small doses at regular intervals, could only state that in view of the possible benefit to be derived, he "did not feel justified in withholding it" from suitable patients.

In the centres I visited in Norway and Sweden (Stockholm, Gotenburg, Lund, Uppsala, Oslo) sanocrysin has not been employed since the years of large dosage and severe reactions, and this applies to some workers in Denmark (e.g. O. Lassen, in Aarhus) who have not given the newer dosage and clearer indications a trial up to the present.

Sanocrysin in Barcelona.

Professor Sayé's work with sanocrysin in Barcelona has attracted much international attention. Two months in his clinics have shown me that added to his enthusiasm is a real attempt to work out the indications and mode of application in a careful and conscientious manner. His results as regards efficacy are probably more telling than those in other countries in view of the inadequate dispensary and sanatorium organization and the low economic level in Spain. Less than one-fifth of his patients can have sanatorium or any form of rest treatment after completion of the course of sanocrysin, during which, however, rest is obtained either in hospital or in their homes. In less than one-third of the sanocrysin patients is some form of collapse-therapy associated. While his indications are based on the effect of the sanocrysin on the early exudative lesion (and he draws special attention to the visibility of the pulmonary network through the X-ray shadow in this connexion), he believes its use to be justified in lesions associated with "acute" cavities, and as a trial measure in moderately advanced caseous and ulcerative cases. He regards as contra-indications old-standing cases with much fibrosis and those showing marked toxæmia or severe tuberculous lesions elsewhere. While administering large single doses ultimately—sometimes as much as 1 grm.—he begins with a small dose, 0·1 grm. or less, guiding himself in this, in subsequent dosage, and as regards intervals, by the weight of the patient, the type of disease, and the reactions obtained. Thus a larger dose, initially and ultimately, will be used for the pure exudative lesion when a curative effect is expected, but small doses will be used in the chronic case with cavitation where the treatment is one "of trial" (*tratamiento de prueba*). The total amount given varies considerably,

but may reach over 20 grm., as Sayé considers that a second course, at least, is advisable even in those patients who improve markedly after the first. Of special interest are Sayé's views on reactions. He divides them into three types. Small or single rises of temperature, slight transient albuminuria, and fleeting erythemas are to be regarded as focal reactions and the next dose given after disappearance of the symptoms. Gastro-enteric disturbances, dermatitis, and persistent albuminuria indicate metallic intolerance and call for an increased interval and the same, or a smaller, dose afterwards. Repetition or multiplicity of intolerance symptoms are due to metallic saturation and compel cessation of treatment. Sayé claims to obtain only 10% intolerance symptoms and rarely experiences saturation syndromes which generally indicate that the patient's prognosis was already unfavourable.

Mention must be made of Sayé's use of sanocrysin for ambulant patients. Included in this series are many patients with small apical shadows in whom the treatment might perhaps be regarded as prophylactic rather than curative, yet in some of them tubercle bacilli have been found in the gastric lavage. His dosage here is smaller—rarely higher than 0·4 grm.—and it is to be noted that the percentage of intolerance symptoms is no higher than in the bed patients.

In the clinic of the late Professor Léon Bernard, at the Dispensaire Léon Bourgeois of the Laënnec Hospital, several hundreds of out-patients, one-third of whom did not stop their work, have now been treated with sanocrysin (or rather crisalbine). Beginning with 0·1 grm., a dose of 0·25 is reached within two weeks, and this dose is repeated weekly for several months. If no improvement results, or in febrile patients, the dose is increased to 0·5 grm. Ten per cent. only of "accidental and incidental diseases" (Charles Mayer) due to the treatment are claimed and this satisfactory result is attributed to the use of 10% calcium gluconate as a solvent for the crisalbine.

Discussion and Conclusions.

In attempting to formulate guiding principles for the use of sanocrysin in pulmonary tuberculosis, failing any conclusive experimental basis of its mode of action, appeal must be made in a certain measure to common sense. The difficulty of collecting reliable evidence as to its effect in man is almost insuperable, for while many individual cases showing improvement or arrest following the use of sanocrysin alone can be brought forward, it is clear that, until such time as the prognosis of every patient can be foretold with accuracy, exact control series—and therefore the rôle played by the sanocrysin—will be unobtainable. In these circumstances we are not justified in withholding the gold salt from those types of cases in which in the past its use has been associated with definite improvement, and the red herring of *nettoyage radiologique* occurring in untreated patients should not be allowed to influence the decision. On the other hand, there seems little justification for the use of sanocrysin as a placebo—for this will imply its use in chronic, fibro-ulcerative cases in which improvement will be difficult to assess, where the treatment may be associated with episodes like hæmoptysis, and as the result of which the mode of treatment is likely to be brought into discredit. I would summarize the clear indications as follows, severe constitutional symptoms to be regarded as a relative contra-indication :—

(1) *Recent lesions* (i.e. those associated with symptoms of not more than three or four months' duration) *of the exudative type* (showing fluffy-edged soft X-ray shadows). When cavitation is present, sanocrysin may be used, but an artificial pneumothorax should be induced without delay.

It is not uncommonly stated that such patients should first be given a trial of three months' sanatorium rest before active measures are adopted. While firmly believing in the efficacy of absolute rest, I can see that this procedure may be somewhat dangerous, in the working and middle classes at any rate, unless our institutional accommodation is sufficient to enable the improvement which may occur at the end of three months to be followed up with continued rest (perhaps six months, a year, or even longer), sufficient to achieve arrest.

(2) The second indication is a *recent exudative lesion occurring in association with old-standing disease.* If this arises in the contralateral side, sanocrysin may be used to eradicate the recent lesion before collapse measures are attempted on the more chronic side, or to deal with a recent exacerbation when the other lung is already collapsed. If serial X-rays are employed, "fresh spreading disease" (Gravesen) on the same side as an old lesion may be detected and sometimes controlled by means of sanocrysin.

(3) A third indication, which I offer tentatively, is the use of sanocrysin for patients in whom suggestive shadows are found during routine examinations (e.g. students, nurses), in the absence of definite clinical evidence of activity, to whom one does not feel justified in recommending a long period of rest which may interfere with their professional career. Observation might be combined with judicious ambulatory gold therapy. This problem will probably loom larger when routine examinations of certain sections of the population are instituted in this country.

As regards dosage, the method of large initial doses appears too dangerous, in view of the severe and occasionally fatal reactions, even if the gravity of the milder reactions has been exaggerated. In a disease which is rarely sufficiently acute for a few days' delay in treatment to matter, there is everything to gain and little to lose by commencing with a small dose, say 0·05 grm., and gradually increasing it by 0·05 grm., and then by 0·1 grm. till a dose of 0·5 grm. is reached. The rule applied by Gravesen as regards intervals appears to be as rational as any, and there seems little foundation for complicated calculations and fine differences. Again, in the present state of our knowledge, Sayé's views as regards reactions and their influence on dosage and intervals appear to be those most acceptable. It is important not to be deterred too soon by mild reactions. Unfortunately, in view of the difficulty in determining when an erythema will develop into a persistent dermatitis, one's situation may often be that between the devil and the deep sea. Finally, if no obvious improvement has occurred after four or six weeks, or about 4 grm. of sanocrysin, there seems little justification for continuing this treatment.

In concluding, may I again emphasize that my remarks are based on observation of the work of others and can at the best only lead to tentative conclusions which I hope, however, may serve to stimulate interest in what is still a highly controversial subject.

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The Hæmostatic Uses of Snake Venom.

By Burgess Barnett, M.R.C.S.

In a short paper published in the *Lancet* of November 3, 1934, there was a preliminary report of the results of an investigation by Dr. R. G. Macfarlane and myself into the possibilities of utilizing the coagulating property of certain snake venoms as a local hæmostatic, particularly in hæmophilic hæmorrhage.

We had utilized the venom of the Russell's viper and found that *very high dilutions* of it clotted blood, both hæmophilic and normal, more rapidly than did any other hæmostatic of our acquaintance.

Since the publication of that paper the venom has had considerable clinical trial at St. Bartholomew's Hospital and elsewhere, and it is with the clinical results obtained at St. Bartholomew's Hospital that the present paper is concerned.

The first two cases cited are ones in which it was used with immediate success:—

(1) F. N. was a hæmophilic man of 43 who was admitted under Professor Gask for a dental extraction for caries on July 18, 1934. He had a previous history of profuse bleeding from slight injuries since the age of 1. Tooth extractions and epistaxis were particularly mentioned as causes of severe hæmorrhage, and he had had frequent hæmorrhages into joints so that flexion of his right knee was limited to 90° and movement of his right elbow was limited.

His brother also suffered from hæmophilia. When he was admitted the platelet count was 220,000; the tourniquet test was negative; bleeding-time was four and a half minutes, and coagulation-time seventeen minutes.

On July 19, the right lower central incisor was extracted under novocain and adrenaline, and the socket was immediately plugged with wool soaked in a 1:10,000 solution of filtered Russell's viper venom. There was no alveolar sepsis.

On account of the adrenaline there was very little initial hæmorrhage before the venom solution was applied, and after the plugging there was no hæmorrhage at all for twenty-four hours. Then the plug was removed, and, apparently, the removal of the plug disturbed the clot, for very free hæmorrhage followed. The plug was replaced by a fresh one soaked in venom and the bleeding stopped practically immediately. In subsequent dental cases a dressing was adopted that hardly amounted to plugging: a piece of wool was shaped like a mushroom with a very short, thin stalk, and was used so that the pressure on it squeezed the venom solution into the cavity, and its removal subsequently did not disturb the clot.

The patient was discharged, at his own request, after the removal of the second plug the following day, and he was given a supply of the venom solution to use if there should be any more hæmorrhage. He wrote later to say that there had been a little oozing twenty-four hours later which stopped at once when he applied the venom.

(2) N. D., aged 4, was admitted under the care of Dr. G. Graham on account of hæmorrhage from a scalp wound. He was a hæmophilic who had bled from slight injuries since the age of 9 months. He had also had hæmorrhages into joints.

The platelet count was 240,000; bleeding-time, four and a half minutes; coagulation time, eleven minutes.

Four of his brothers were hæmophilics, and two of them had died from hæmorrhage. There was a family history of the disease, going back for three generations.

Four days before admission he had fallen against the edge of a gas-stove and had bled nearly continuously since then from a triangular cut which extended down to the periosteum. The wound was not septic. It was dressed with gauze soaked in the venom solution, and the bleeding stopped immediately. Twenty-four hours later, a little bleeding necessitated a second dressing, and again after thirty-six hours, when it finally stopped. The wound healed in ten days.

The following four cases are of hæmorrhages in hæmophilics which presented a certain amount of difficulty. In each of them the difficulty was the mechanical one of the application of the venom solution to the bleeding part; the clot was always formed at least as rapidly as would have been the case in normal subjects.

(3) G. F., a man, aged 24, was admitted for dental extraction on November 23, 1934, under Dr. Hinds Howell.

He had bled from childhood from slight injuries, and into his joints. Four brothers were hæmophilics, three of them had died as a result of hæmorrhage. A cousin and a nephew were also hæmophilics.

On admission his hæmoglobin was only 58% and he was detained for a fortnight, until the hæmoglobin was 86%, before the extractions were performed. Two teeth, six and seven of the right upper jaw, were removed on December 5. Regional block anæsthesia was used without adrenaline. There were very foul alveolar abscesses, and the stench from them was perceptible outside the ward. The septic cavities were plugged with venom solution, but although good firm clots were formed, oozing continued and plugging with venom had to be repeated every three hours to control it. The next day venom plugging was resorted to every six hours. Later a dental plate was made to retain the plugging in place, and hæmorrhage finally ceased after five days. A week later the hæmoglobin was 80%.

The next case is similar to the last:—

(4) W. L., a hæmophilic, aged 30, was admitted under the care of Professor Gask and Dr. Graham, for extraction of a tooth, with an alveolar abscess, on October 3, 1934. Two of his brothers were hæmophilics, one of these had died from hæmorrhage; four maternal uncles were bleeders. The platelet count was 198,000; the tourniquet test was negative; the bleeding-time was four minutes and the coagulation time varied from thirteen to thirty-five minutes.

There was the usual history of repeated bleeding from small injuries and the patient was more or less crippled from hæmorrhages into joints. On several occasions he had nearly bled to death.

On the day of admission an upper right incisor was extracted under a local anæsthetic with adrenaline, and the socket was plugged with venom solution. There was no hæmorrhage for ten hours, but after that replugging with venom was necessary to control bleeding. Replugging was repeated twice daily for four days. The sockets were very septic, but healing was complete in six days.

On admission, the hæmoglobin was 72%; it never fell below 60%. While in hospital there were subcutaneous hæmorrhages into the buttock and the right eye, which appeared to be in no way connected with the use of the venom.

The next case illustrates another point.

(5) J. L., a hæmophilic, was admitted under Dr. Graham on account of a cut on the dorsum of the right hand.

The platelet count was 240,000; the tourniquet test was negative; bleeding time was three minutes, and coagulation time, six minutes. There was the usual history of repeated profuse hæmorrhages.

He had cut his hand two days previously and bleeding had been continuous since then. On admission there was a large hæmatoma. This was evacuated: a spurting artery was ligatured, and other bleeding was controlled with venom solution. The wound was then closed by sutures. The following day an enormous hæmatoma, rendering the hand almost spherical, was formed, and there was copious oozing. The stitches were removed and the liquid blood forming the hæmatoma was evacuated. Hæmorrhage was now very profuse, but when a light dressing of gauze soaked in venom solution was applied the bleeding stopped at once. The wound was allowed to granulate up from below without skin sutures and there was no more hæmorrhage.

Subsequently the same patient had a septic molar stump removed, with much the same history as that of the other septic dental cases, except that hæmorrhage was more easily controlled by means of a dental plate that was made for him.

(6) The next hæmophilic case to be mentioned is one in which the only difficulty was mechanical. It was that of a boy, aged one year and a half, who was admitted under Professor Gask on account of hæmorrhage, following a bitten tongue. It was not previously known that he was a hæmophilic, but he had a coagulation time of six minutes. On account of the child's movements it was impossible to retain the dressing on the tongue and he lost so much blood that two transfusions were performed. Ultimately a dental plate was made and fixed over the tongue so as to hold the venom-soaked dressing on the tongue. The hæmorrhage then ceased.

(7) One of the hæmophilic patients already mentioned, W. L., has had epistaxis controlled by venom solution on several occasions, with complete success. On each occasion, after the nasal cavity had been washed out, the anterior nares were lightly plugged with ribbon gauze soaked in the venom solution and hæmorrhage stopped almost immediately. After a few hours the plugging was removed and a second dressing was never necessary.

In all the above cases the venom always produced coagulation as rapidly as could be desired; it formed as firm and elastic a clot as that of normal blood—very different from the thin, friable ones characteristic of hæmophilia. Where there was difficulty it was the mechanical one of sealing the bleeding point with the venom-formed clot.

The only patient under our observation who had an abnormal blood condition other than hæmophilia was a boy aged 4 years, suffering from purpura hæmorrhagica, who was treated for epistaxis. The platelet count was 60,000; bleeding time thirty minutes; the tourniquet test was positive and the coagulation time was normal. On several occasions epistaxis was stopped immediately by plugging the anterior nares with venom-soaked ribbon gauze.

Over a period of some seven months the venom solution has been employed constantly in the dental department at St. Bartholomew's Hospital, in cases of severe hæmorrhages following extractions from patients with normal blood. It was successful in all cases except two. One of these I have no account of, but in the other the excretion of ascorbic acid in the urine was below normal and it appeared that the patient was suffering from subclinical scurvy.

In general surgery the venom solution has been employed by Professor Gask to stop capillary oozing after the breaking-down of adhesions from the surface of the liver, and in another case after the capsule had been stripped from a kidney. It has also been used by Mr. M. Boyd successfully after tonsillectomy, and by Mr. H. W. Wilson after prostatectomy.

In all cases the venom has been employed in a strength of 1 : 10,000, and in none of them have there been any toxic symptoms that could be attributed to it.

Section of Surgery

President—PHILIP TURNER, M.S.

[*April* 3, 1935]

DISCUSSION ON TRAUMATIC SHOCK

Mr. R. L. Holt: In recent years the term shock has been used to describe the state of circulatory failure or depression which is presented by patients suffering from a diversity of lesions, but this evening the discussion is limited to traumatic shock and by that, it is presumed, is meant the shock which follows direct injury to the body tissues.

It has been the custom to divide cases of shock into primary and secondary types, depending on the rapidity with which the state of shock develops after the receipt of injury. There is much to be said against such a classification, but for the greater part of this contribution shock will be referred to as primary or secondary in type.

Secondary shock.—Secondary shock is the more common and important of the two types and accordingly will be considered first. The clinical features of this type are well known. The cold skin, the pallid lips, the shallow, feeble respirations, the bluish finger nails, the sweating, the thirst, the apathy, the rapid pulse, and low arterial blood-pressure present an unmistakable picture. The post-mortem appearances in animals which have died from traumatic shock are equally characteristic. The pallor of the viscera is striking, and is especially well-marked in the intestines and omentum. This is not entirely due to the low blood-volume but, in part, to the intense vaso-constriction which is always evident in this type of shock. The essential pathological feature of this condition is a diminution in the volume of circulating blood—a point which was brought out by Robertson and Bock [1] and later emphasized in the clinical researches of Keith [2]. Any theory which satisfactorily explains the pathology of secondary shock must account not only for the fall in arterial blood-pressure, but also for the diminution of the blood-volume. The majority of the earlier theories have been discarded because they failed to explain these two changes. The only theory which, until recently, appeared to satisfy these conditions was the "traumatic toxæmia" theory which was suggested by Quénu [3] and by the Committee appointed by the Medical Research Council in 1917 to investigate the pathology of shock.

Theory of Traumatic Toxæmia

The experimental work which formed the basis of the theory of traumatic toxæmia was performed on anæsthetized cats, and shock was produced by traumatizing one of the hind-limbs. This method of producing shock was undoubtedly suggested by the fact that both in war and in civil practice secondary shock is characteristically seen in association with injuries causing extensive damage to muscle tissues. Cannon and Bayliss [4] found that the low blood-pressure which resulted from such trauma occurred whether or not the spinal cord or the nerves to the

limb had been severed prior to the trauma. They amputated the two hind-limbs symmetrically through the upper part of the thighs and, from comparative weighings, concluded that the loss of blood and plasma into the damaged tissues was insufficient in itself to account for the fall in blood-pressure. They found that by clamping the main artery and vein to the limb before trauma was applied, collapse of the circulation was delayed until the clamps were removed. They concluded, therefore, that a substance was produced in the damaged tissues which, on absorption into the circulation, resulted in a fall of blood-pressure. They regarded their results as analogous to the effects produced by the intravenous injection of tissue extracts, and Cannon quoted the work of Dale and Laidlaw [5] who had previously described a shock-like condition produced in animals by the injection of histamine. This condition bore so close a resemblance to that produced by muscle trauma that it seemed to Cannon reasonable so suppose that histamine and the hypothetical depressant of the traumatic toxæmia theory were at least closely related substances.

Criticisms of the traumatic-toxæmia theory.—This theory, although widely accepted at the time of publication, has since been severely criticized. Against it is urged:—

(1) That no observer has satisfactorily demonstrated the presence of any depressor substance in the venous blood from a traumatized area.

(2) That the circulatory changes of traumatic shock differ considerably from those produced by the injection of histamine or other depressor substances obtained from tissue extracts.

(3) That the comparative weighings of the normal and traumatized limbs, as practised by Cannon and Bayliss [4], failed to give a true picture of the extent of the extravasation and hæmorrhage into the damaged area.

The experimental work reported below fully supports these criticisms.

Experiments Showing Absence of Depressor Substance in Blood from Traumatized Area

The first group of experiments to be described were carried out about eighteen months ago by Macdonald and myself [6], repeating some of the work which M. I. Smith [7] published in 1928. Anæsthetized dogs were used throughout the experiments, and records of blood-pressure were taken in the usual way. Shock was induced by striking the thigh and gluteal muscles with the flat side of a hammer. By inserting a three-way cannula into the iliac vein it was possible to withdraw either most or any part of the blood returning from the experimental limb during or after trauma. 60 c.c. of blood were collected during the latter part of a shock-producing trauma and were reinjected as soon as the blood-pressure became steady. This raised the blood-pressure, although the sample was taken during a steep fall when the likelihood of a spread of any depressor substance present was at its greatest. In no experiment of this kind in which blood from a traumatized limb was collected and reinjected was any evidence found of the presence in that blood of any histamine-like substance. The same conclusion was arrived at if the blood was transferred to another animal in which no trauma had been induced. On the other hand, if the common iliac vein was clamped and 1 mgm. of histamine injected into the iliac artery of the same side and a small sample of blood, 5-10 c.c., collected from the vein even ten minutes later, such blood on reinjection produced a typical histamine response—a sharp fall in pressure, with recovery a few minutes later.

These results confirm Smith's [7] claim that "direct methods have failed to demonstrate a depressor substance in the blood of the shocked animal." A similar conclusion was reached by Parsons and Phemister [8] and more recently by Slome and O'Shaughnessy [9].

Differences between Circulatory Changes of Traumatic Shock and those following Histamine Injection

The second criticism of the traumatic-toxæmia theory is rather indirect, since it assumes that histamine is the toxin produced in the injured tissues. Blalock [11] showed that after muscle trauma the output of the heart diminished considerably before a definite alteration in the blood-pressure took place, and Burch and Harrison [12] have shown that after histamine injection there is first of all a decline in the blood-pressure and the cardiac output is only subsequently diminished. Roome, Keith, and Phemister [10] showed that it was necessary to remove much larger quantities of blood to cause death in experiments in which shock had been produced by the injection of histamine than in those in which shock had been produced by hæmorrhage or muscle trauma. Confirmation of these differences is found when the post-mortem appearances in animals dying of traumatic shock are compared with those in animals whose death is caused by histamine injection. In the former there is a general pallor of the abdominal and thoracic viscera; in the latter the viscera appear congested and the solid organs bleed freely on section. It appears, therefore, that some mechanism other than the liberation of a histamine-like substance and its absorption into the circulation must be responsible for the production of shock.

Experiments Proving Importance of Local Fluid Loss into the Traumatized Tissue.

The third criticism of the conclusions of the theory of traumatic toxæmia is more helpful, since it provides the basis on which the pathology of secondary shock is explained by recent workers. Cannon and Bayliss [4] concluded from their work that following trauma to one of the hind-limbs of an animal there was never sufficient bleeding into the wounds to account for the effects observed. They amputated the limbs through the upper ends of the thighs, but Blalock [13] pointed out that the extravasation of blood and plasma following trauma to a thigh, extended upwards into the loose tissues of the groin and flank. When these tissues were included in the amputation it was found that the difference in the weights of the limbs amounted to half of the initial total calculated blood-volume. Our second group of experiments were a repetition of those reported by Blalock [13] in 1930. Shock was induced, as in the previous experiments, by traumatizing one hind-limb. Then, after the animal had died or been killed, its hindquarters were removed by an amputation through the lower lumbar regions. The hindquarters were then divided, great care being taken to see that this was done symmetrically and the two halves weighed. Tables I and II represent typical results from our experiments. The difference in weights of the traumatized and control limbs amounted to about 45% of the total blood-volume—a figure much higher than the 11% obtained by Cannon and Bayliss [4]. The nature of the fluid extravasated into the injured tissues has been shown to be a mixture of blood and plasma, and such a rapid loss from the circulation is quite sufficient to account for most of the phenomena of secondary

TABLE I.—TYPICAL EXAMPLES OF SHOCK FOLLOWING TRAUMA IN THE DOG

Experiments	Dog's weight in kilos.	Initial blood-pressure mm. Hg	Shocked blood-pressure mm. Hg	Difference in limb weights calculated in percentage of animals' total blood
1	8	130	70	30
2	7½	140	85	43
3	7	165	85	60
4	10½	175	55	57
5	7	150	65	63
6	9	160	40	45
7	9½	165	60	33

Average percentage of blood-volume lost in traumatized area = 47

TABLE II.—TYPICAL EXAMPLES OF SHOCK FOLLOWING TRAUMA IN THE CAT

Experiments	Initial blood-pressure mm. Hg	Shocked blood-pressure mm. Hg	Difference in limb weights calculated in percentage of animals' total blood	Survival (hours)
1	160	—	44	3
2	145	95	61	3¼ destroyed
3	190	—	49	4
4	180	—	40	2
5	165	105	53	5 destroyed
6	140	40	48	3¾ destroyed
7	168	—	64	4
8	180	—	35	5
9	185	50	43	5¾ destroyed
10	190	—	14	1¼

Average loss 45% of calculated initial blood-volume.
Blood volume calculated as 5·75% of body-weight.

shock. Our experiments provide ample confirmation of Blalock's [13] contention that following muscle trauma the extravasation of fluid into the damaged tissues is always sufficient in amount to account for the fall in blood-pressure.

The experimental work referred to has so far been concerned with shock resulting from muscle trauma. The importance of this factor of local fluid loss is not restricted to shock so produced, but has been shown by Blalock to be responsible in large part for the secondary shock resulting from extensive burns [14] and intestinal manipulation [15]. The simplest example of shock produced as a result of a diminished blood-volume is that following hæmorrhage, and the circulatory changes in the shock so produced are exactly the same as those resulting from muscle trauma [18]. There is every reason, therefore, for believing that the factor of local loss of blood and plasma is the most important factor in the pathology of traumatic shock.

The Part Played by Nervous Impulses from the Injured Tissues

The fall in blood-pressure following muscle trauma comes on so quickly as to suggest that it might be of neurogenic origin. Macdonald and I [6] investigated the cause of this initial fall, believing that it might produce further evidence of the changes taking place in the traumatized tissues. It was found that the fall in blood-pressure after mild trauma occurred (*a*) when all nerve impulses had been cut off by means of a spinal anæsthetic, and (*b*) when the common iliac vein was occluded. The fall was only prevented by occluding the iliac artery. These findings suggest that even the initial fall in blood-pressure is the result of a local change, presumably an opening up of the large vascular bed provided by the muscles of the limb. The cause of the vaso-dilatation is not evident. If it be due to the action of a vaso-dilator, such action is entirely local, since there is no evidence of the passage of such a substance into the general circulation.

The majority of experimental workers are agreed that denervation of the limb, including sympathectomy, or transection of the cord, does not prevent the development of secondary shock following trauma. Recently, O'Shaughnessy and Slome [9] have suggested that the nervous system plays an important rôle and have brought forward evidence to show that the induction of spinal anæsthesia before the limb is traumatized, delays or prevents the onset of shock. Macdonald and I [6], as previously mentioned, showed that spinal anæsthesia fails to prevent the initial fall in blood-pressure. In a later series of experiments the evidence obtained does not support the view that "nociceptive nervous stimuli from the injured tissues dominate the picture." A comparison of Tables II and III does not support the suggestion that spinal anæsthesia exerts a beneficial action on the development of shock following trauma. With the possible exception of Experiment 10 in Table II no evidence was found in our experiments to suggest that the

TABLE III.—TYPICAL EXAMPLES OF SHOCK PRODUCED IN CATS BY MUSCLE TRAUMA AFTER INDUCTION OF SPINAL ANÆSTHESIA

Experiments	Initial blood-pressure mm. Hg	Shocked blood-pressure mm. Hg	Difference in limb weights calculated in percentage of animals' total blood	Survival (hours
1	135	110	40	5½ destroyed
2	165	—	53	50 minutes
3	190	—	35	2½
4	130	80	51	2½ destroyed
5	195	55	44	2 destroyed
6	180	—	53	1½
7	195	—	73	1½
8	170	100	60	2½ destroyed
9	180	—	47	2½
10	195	—	53	2½
11	165	—	44	3½
12	155	—	36	1½
13	155	65	48	2¾ destroyed
14	145	—	48	3½
15	130	—	27	3½
16	155	60	40	3½ destroyed
17	110	70	47	6 destroyed
18	150	—	48	¾

Average percentage of blood-volume in traumatized area 48.
Blood-volume calculated as 5·75% of total body weight.

importance of a neurogenic factor compared in any degree to that of the factor of local fluid loss.

In the same paper O'Shaughnessy and Slome [9] have suggested that the induction of spinal anæsthesia in an animal already in a severe state of shock results in a rise in the blood-pressure. This has not been our experience. In fact in severe cases of shock it appears as though the induction of spinal anæsthesia hastens the fatal result. It has certainly been my experience clinically that it is a most hazardous proceeding to give a spinal anæsthetic to a patient who is in a state of shock or dehydration without first of all carrying out measures to bolster up the blood-volume.

Factors Tending to Aggravate or Maintain Shock

It is not contended that the factor of local fluid loss is the whole story of secondary shock. Under certain conditions, such as a severe hæmorrhage or very extensive trauma, this factor alone may be sufficient to cause death, but otherwise the local fluid loss is to be regarded as the initiating factor of secondary shock. It is easy enough to produce a fall in blood-pressure experimentally by muscle trauma but unless the trauma is severe the low blood-pressure is not maintained. The healthy animal shows a strong tendency to recovery and it does so by drawing on the large fluid reserves stored up in the tissues. That such a change takes place was shown in some of our experiments in which dilution of the blood was found to occur after trauma. It naturally follows that any factor which lessens the fluid reserves, or which retards their passage into the circulation, will exert a powerful influence on the development and maintenance of shock. The susceptibility to shock may be increased by lack of food and water and by illnesses, particularly those associated with vomiting. Exposure to cold, sweating, and vomiting are potent forces in reducing the volume of tissue fluid available and are factors which, clinically, are commonly present in patients suffering from shock. Lastly, Freeman [16] has recently pointed out that many of these factors have one action in common, and that is to stimulate the sympatho-adrenal system. He has shown experimentally that the continuous injection of adrenalin in physiological amounts over from two to three hours reduces the blood-volume by 20% or more. Vaso-constriction, normally a protective mechanism, has an adverse effect when long-continued, by causing a further reduction in the blood-volume.

Summary of Pathology of Traumatic Shock

It is possible, with all the above-mentioned facts available, to outline the pathology of traumatic shock. The bulk of evidence brought forward has been obtained from work on anæsthetized animals, and conclusions can only be drawn with the usual reservations. No mention of the factor of pain has been made, because it is not possible in experimental work on animals to obtain any reliable results. But it is known that pain frequently results in stimulation of the sympatho-adrenal system, the effects of which have already been mentioned. The initiating factor of secondary shock is a reduction in the blood-volume which results from the loss of blood and plasma into the injured tissues. This results in a diminished output of the heart, an increased pulse-rate, vaso-constriction and, lastly, a fall in arterial blood-pressure—a purely physiological defence of the circulation of the vital structures. A further reduction in the blood-volume, which may result from the many influences mentioned as maintaining factors, produces a further fall in arterial pressure. The prolonged vaso-constriction may further reduce the blood-volume and in this way is set up a vicious circle which accounts for the progressive nature of fatal shock. The vaso-constriction, most marked in the skin and splanchnic area, provides a plausible explanation of the dusky skin, the bluish finger-nails, the high red-cell count of capillary blood, and the clogging of the capillaries of the intestinal villi which are so typical of secondary shock. In a pronounced state of shock the circulation cannot be maintained efficiently and it is probable that many of the tissues suffer from anoxæmia. In the capillaries this will increase their permeability and in the nervous system the more susceptible tissues may have their functions impaired. These two latter factors are probably the cause of the disappointing results obtained in the treatment of the late cases of shock.

Primary Shock

To complete the picture of traumatic shock there remains to be considered the question of primary shock, which is generally regarded as being neurogenic in origin. It has been shown, however, that the initial fall in the blood-pressure which follows muscle trauma is independent of the central nervous system. True neurogenic shock is very different [17]. It is seen typically in the fainting which occasionally accompanies emotional distress or trivial injuries. A similar circulatory collapse is sometimes seen when the upper abdomen is opened and in conjunction with operations on the brain. The circulatory collapse is explained by a sudden inhibition of vaso-constrictor tone of central origin. It is interesting to note that in this type the blood-pressure may remain too low to be recorded for an hour or more, and then may pick up spontaneously with no apparent ill-effect. A similar fall in blood-pressure in a case of secondary shock would be a matter of grave concern. The explanation of this difference lies in the character of the circulatory changes in the two conditions. In secondary shock a marked fall in blood-pressure is serious, implying such a reduction in the volume of circulating blood that an intense vaso-constriction is unable to maintain the pressure. In neurogenic shock a fall in blood-pressure has not the same significance ; there is no reduction in blood-volume and if the circulation to the susceptible medullary centres, e.g. the respiratory centre, be maintained, no ill-effect results. Generally these depressor reactions of neurogenic shock are transient and of minor importance, but fatal cases do occur in which the blood-pressure falls early and without any evident cause. Then it is difficult to rule out a nervous factor.

The division of shock into primary and secondary types is obviously artificial and open to criticism. The adoption of a classification, which has an ætiological basis, is clearly desirable. Blalock [11] and other American writers recognize the following types :—

(1) Hæmatogenic—shock resulting from loss of circulating blood, e.g. hæmorrhage muscle trauma.

(2) Neurogenic—shock resulting from loss of central vascular tone, e.g. trivial injury, emotional disturbance, &c.

(3) Vasogenic—shock resulting from loss of peripheral vascular tone, e.g. histamine and other drug reactions.

It is suggested that the general adoption of such a classification will help to reduce the present confusion and lead to a readier understanding of the important factors which contribute to the ætiology of shock.

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Dr. David Slome: The interpretation of the phenomenon of circulatory collapse that follows trauma can be approached from two view-points. Thus it is possible to distinguish two classes of hypotheses, which are not necessarily mutually exclusive. One class is concerned with the general somatic changes which constitute the syndrome. The other is concerned with establishing a link between the traumatized area and the body as a whole. The latter is, of course, the primary ætiological problem, since all the general bodily changes are dependent upon the operation of this link.

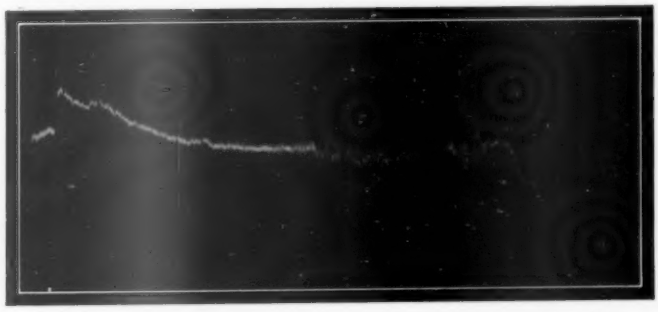


Fig. 1.—Trauma to thigh. Cat 92. 3,000 grm. chloralose. Tracheotomy. Initial blood-pressure 135. Signal: Trauma to thigh. Death two hours twenty minutes after trauma. 53 grm. increase in weight of traumatized limb. Time signal 30 seconds.

This link may be either vascular or nervous. There are two aspects of the vascular link: (1) The mechanical loss of fluid into the area of trauma; (2) the introduction into the general circulation of a chemical product or toxin from the injured tissues.

Thus the syndrome of traumatic shock might be attributed to the operation of one of three factors or a combination of two or all of these. These are: (1) A toxin

elaborated in the area of trauma and passed into the general circulation either through vascular or lymphatic channels; (2) fluid loss at the site of trauma; (3) the discharge of nerve impulses from the area of trauma. Figure 1 (p. 73) illustrates the problem.[1]

In these experiments, carried out by Mr. O'Shaughnessy and myself, trauma was inflicted by blows on the thigh muscles of the anæsthetized cat, producing fracture of the femur. This blood-pressure tracing (fig. 1) shows the gradual decline of the pressure, with the development of shock. The animal died after two hours and twenty minutes. In the majority of the control experiments death occurred within three and a half hours after trauma.

Theory of Traumatic Toxæmia

The brilliant pioneer researches of Sir Henry Dale demonstrated the shock-like state produced by large doses of histamine, and the presence of this and other depressor substances in the tissues. Dale was careful to point out the important respects in which the circulatory collapse of histamine poisoning differed from that following trauma. In a paper in 1920 he said: "There has been evident in certain recent publications a tendency to attribute to this resemblance in action a chemical significance for which we found and for which I still find insufficient justification." Nevertheless, there was a strong tendency, following the researches of Cannon and Bayliss, for the toxic factor to be regarded as the main and most important agent in the production of the shocked state.

Cannon and Bayliss demonstrated that the fall of blood-pressure which develops after trauma to the thigh in animals fails to occur if ligatures are applied to the vessels of the limb prior to trauma. If, later, the ligatures are removed, shock develops. They explained this, by the inability of the vasodilator toxins, to pass into the general systemic circulation till the ligatures are removed. This result is, however, equally explicable on either of the other two hypotheses. The occlusion of the blood-vessels prevents the fluid loss, and in the presence of such intense anæmia the conduction of impulses along the nerves may be suppressed.

The following experimental findings can be cited against the toxic theory:—

(1) *The quantity of histamine and other toxins in the traumatized muscle is inadequate to cause shock.*

It is an assumption implicit in the toxic hypothesis that the quantity of these toxins in the damaged tissues must clearly be sufficient in amount to produce shock. Muscle has a very low content of depressor substances. The amount of these substances necessary to produce shock in an animal could be obtained only by careful extraction from a mass of muscle greater than the entire weight of the animal. The difficulty of assigning to the damaged muscle the rôle of producing sufficient toxins to cause a lasting fall of pressure cannot therefore be lightly dismissed.

(2) *Occlusion of the venous return from a traumatized limb does not prevent shock.*

In the experiment illustrated in fig. 2, the right common iliac vein was divided between ligatures. Histamine introduced into a tributary of the right femoral vein still produced its characteristic effect. To ensure effective occlusion of the venous return, we found it necessary to carry out an extensive series of ligatures. When the venous return was completely blocked in this way traumatic shock could still be produced (fig. 3). These experiments do not dispose of the possibility that the hypothetical toxin might be absorbed along lymphatic channels. This possibility of lymphatic absorption must also be entertained in relation to the experiment described by Mr. Holt, in which blood was collected from the femoral vein.

[1] Figures 1, 2, 4-11, 14, 15, 16, are reproduced from the *British Journal of Surgery*, 1935, by kind permission of Messrs. John Wright and Sons, Ltd.

(3) *Perfusion of the area of trauma fails to elicit any evidence of the presence in traumatized tissues of vasodilator substances.*

Fig. 4 illustrates, diagrammatically, the method of perfusion. A cannula was inserted into the peripheral end of the femoral artery and connected to a flask from which saline was supplied at constant rate and temperature A clip was placed on the femoral vein and the limb was traumatized. At definite periods after trauma

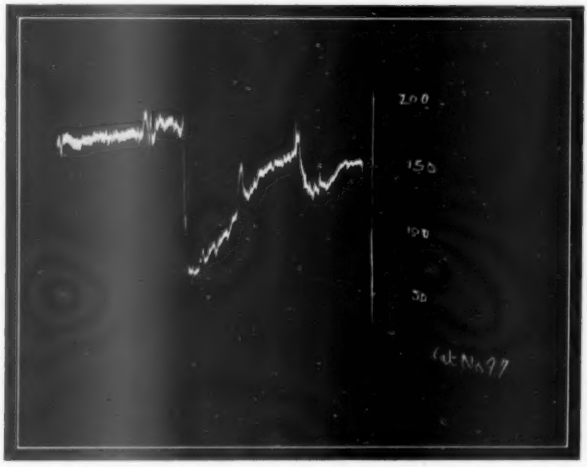


FIG. 2.—Ligation of common iliac vein and injection of histamine. Cat 97. 2,500 grm. Chloralose. Tracheotomy. Initial blood-pressure 170 mm. Hg. Signal 1-2: Ligatures on right common iliac vein and section of vessel. Signal 3: 1 mgm. histamine injected into tributary of right femoral vein. Blood-pressure falls to 75 and recovers. Time signal 30 seconds.

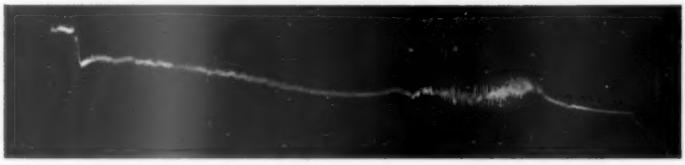


FIG. 3.—Development of traumatic shock despite complete occlusion of venous return from limb.

the clip was removed and saline run in. A rise in blood-pressure and not a fall resulted. A possible criticism is that the pressor effect of the saline infusion neutralized the depressor effect of any toxin present. As a control, therefore, histamine was introduced into the traumatized area and the perfusion repeated; an immediate fall of pressure was produced (fig. 5).

We also found that if histamine was put into a *traumatized* thigh, and then washed into the circulation, the fall of blood-pressure was no greater than that which resulted in a similar experiment using an equivalent dose of histamine in an *untraumatized* thigh.

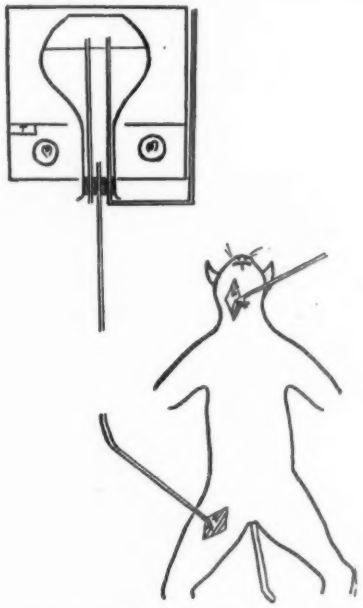


FIG. 4.—Perfusion of limb experiment.

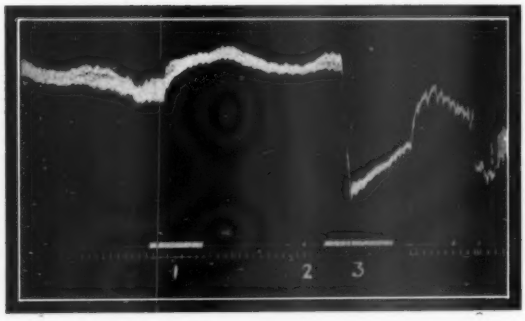


FIG. 5.—Cat 2. Saline perfusion of traumatized limb. Trauma to thigh—vessels clipped. Signal 1: Perfusion of traumatized limb 30 minutes later. Signal 2: 2 mgm. histamine into traumatized area. Signal 3: Perfusion of traumatized limb. Time signal 30 seconds.

(4) If the toxin is absorbed along either venous or lymphatic channels its presence in the *general* circulation should be demonstrable. In the search for toxic substances in the general circulation we used a method based on vividialysis.

Fig. 6 is a diagram of the apparatus designed for this purpose. The carotids of two animals are attached to the apparatus. The blood of one enters at R, passes through the collodion tubes P and Q and back to the same animal. The blood of the other enters at D, passes outside the collodion tubes and back through E. The circulations, therefore, remain distinct, but are separated within the apparatus only by the collodion membranes, across which substances can diffuse.

Using this apparatus we found that: (1) Trauma to one animal is without effect on the blood-pressure of the other (fig. 7); (2) slow intravenous infusion of

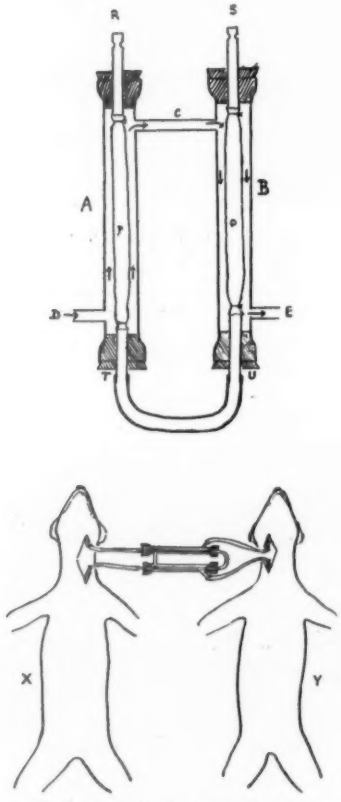


FIG. 6.—Vividialysis experiment.

histamine maintaining the pressure of one animal at a shock level is accompanied by a fall of pressure in the other (fig. 8).

(5) Lastly, the post-mortem appearances in animals whose death has followed the administration of histamine are characteristic and differ significantly from those after trauma. The dilated vascular bed after histamine poisoning is noticeably absent in traumatic shock (figs. 9, 10). These facts weigh heavily against the

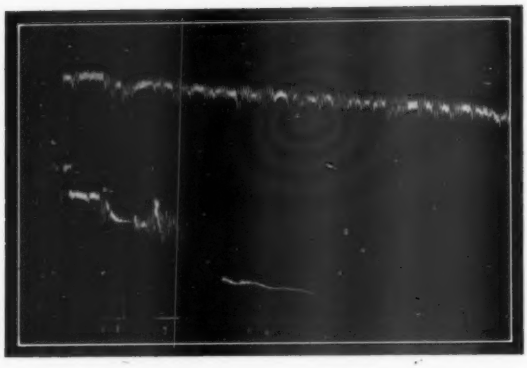


FIG. 7.—Dogs 1, 2. Vividialysis: Trauma. Each dog weighed 1,500 grm. and the anæsthetic was morphia-and-nembutal. The two animals were connected to the dialyser and the circuits opened at signals 1 and 2. Dog 1, lower curve; dog 2, upper curve. Signal 3: Trauma to dog 1. The traumatized dog went into shock and died thirty minutes later, while the blood-pressure of dog 2 remained unaffected. Time signal 30 seconds.

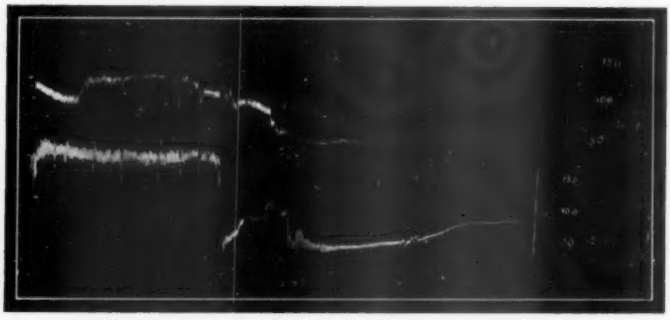
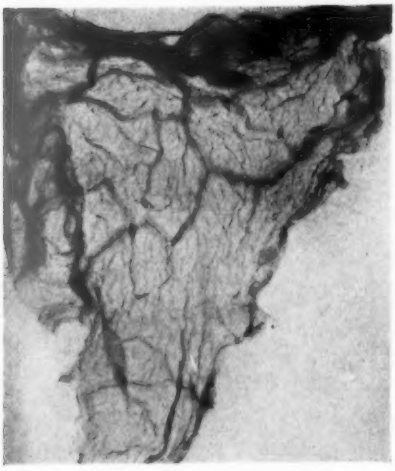
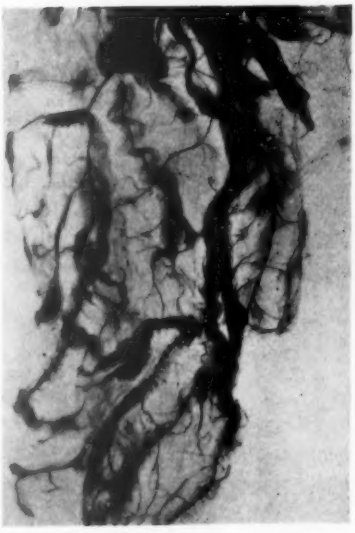


FIG. 8.—Dogs 7, 8. Vividialysis: Histamine poisoning. Two dogs anæsthetized by morphia-and-nembutal connected to the dialyser and at signal 1 circuit opened. Dog 7, lower curve; dog 8, upper curve. Initial blood-pressure: dog 7, 170; dog 8, 130. Signals 2-7: Successive doses of 5 mgm. histamine in 10 c.c. water injected into the femoral vein of dog 7. An immediate fall in blood-pressure which was maintained at a level of 40-60 for about an hour. The blood-pressure of dog 8 declined, and fifteen minutes after the injection of histamine into dog 7 it was at 60, and forty-five minutes later dog 8 died. Both showed at autopsy the evidences of histamine poisoning.



A

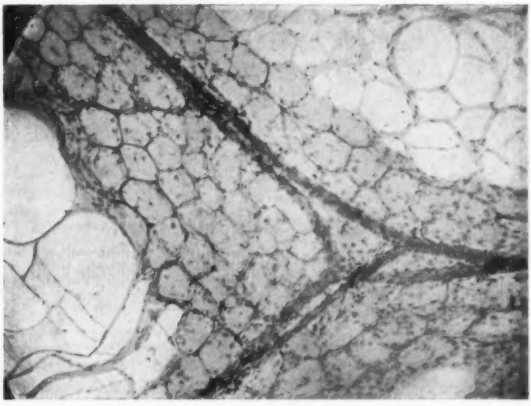


B

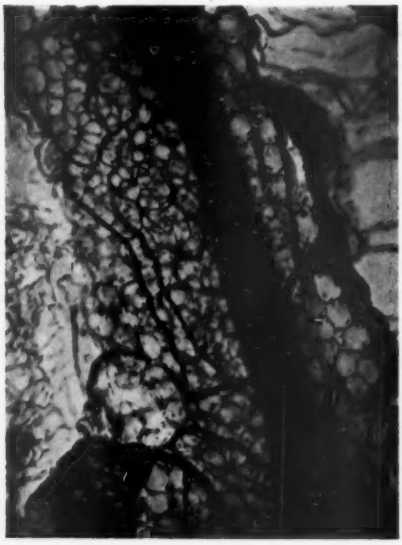
FIG. 9.—Macroscopic specimens of omentum in: A, Traumatic shock; B, Histamine poisoning.

conception of a humoral agency as a significant causal factor in the development of traumatic shock of this type.

Histamine causes capillary dilatation and stagnation and has given rise to the idea that the shocked person "bleeds into his own capillaries." Until it is unequivocally established that in the shocked person the capillaries are dilated, this phrase cannot be justified. In fact, the extreme pallor of the shocked patient suggests that the capillaries of the skin, at any rate, are not dilated.



A × 80.



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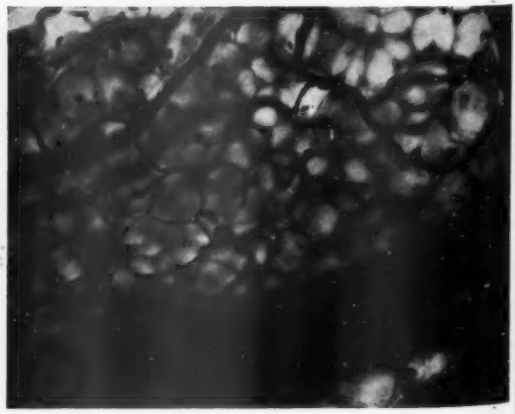


B × 190.

FIG. 10.—Microphotographs of omentum in: A, traumatic shock; B, histamine poisoning.

Fluid-Loss Theory

The view that the fluid loss due to extravasation of blood and exudation of plasma at the site of trauma is sufficiently great to account for the development of shock has been ably presented by Mr. Holt in his opening paper.

Complete occlusion of the blood-supply to a limb prevents the development of traumatic shock (fig. 11).

The average fluid loss in our experiments was 36% of the calculated total blood-volume. Fluid loss is undoubtedly an important factor. This view takes us back in a sense to the old surgical doctrine—"Shock is hæmorrhage and hæmorrhage is shock." That shock is hæmorrhage is true, but is it only hæmorrhage? There are certain findings that strongly suggest that in addition to fluid loss some other factor is present.

FIG. 11.—Trauma to thigh after ligation of vessels. Cat 25, 3,000 grm. chloralose. Tracheotomy. Initial blood-pressure 190. Signal: Trauma to thigh. Killed five hours later with a blood-pressure of 180. Difference in weight of limbs, 17 grm. Time signal 30 seconds.

(1) In some of our experiments the fluid loss amounted to only about 20% of the total blood-volume. Nevertheless, the onset of shock was comparable, both in severity and in the rapidity with which death occurred, with the other cases. A comparison of cats, 69 and 92 in Table I, emphasizes this fact. The degree of fluid

TABLE I.—CONTROL EXPERIMENTS

Cat No.	Weight of cat	Increase in weight of traumatized limb	Fluid loss expressed as a percentage of calculated blood-volume	Initial blood-pressure	B.P. after one hour	Survival time
	Grm.	Grm.		mm.Hg.	mm.Hg.	Hours
69	1,500	55	48%	160	60	4½
78	2,500	58	30%	195	150	3
88	2,750	—	—	180	140	3½
83	3,000	130	56%	160	20	1½
50	3,200	56	22%	170	50	2½
76	4,250	—	—	165	150	6½
20	3,000	69	30%	165	90	2
92	3,000	53	22%	135	110	2

loss into the traumatized tissues does not bear any direct relationship to the survival time. Unless there is some other factor one would have expected that the greater the fluid loss, the more rapidly death would take place.

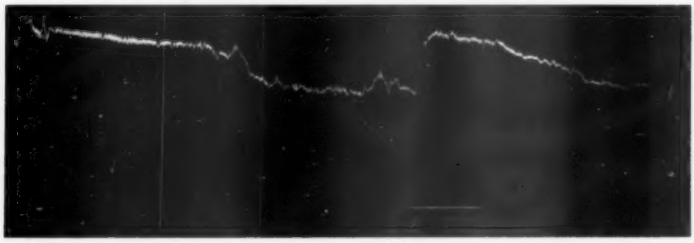


FIG. 12.—Trauma: Blood transfusion. Cat 137. Chloralose. Initial blood-pressure 130 mm. Hg. Signal 1: Trauma. Blood-pressure falls to 77 mm. of Hg. Signal 2: Blood transfusion 50 c.c. After half an hour blood-pressure again fallen to 80 mm. Hg. Increase in weight of traumatized limb 56 grm.

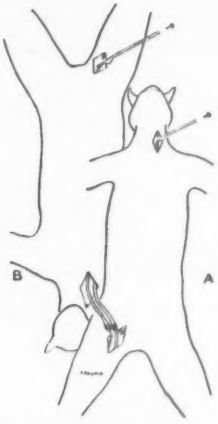


FIG. 13A.—Diagram of cross circulation experiment.

(2) Blood transfusion will not permanently relieve shock (*see* fig. 12).

(3) Trauma to the limb of an animal supplied with blood from a second animal will produce shock in the first animal, though only nervous pathways are intact (figs. 13A and 13B).

The Nervous Factor

The relation of the nervous system to traumatic shock is demonstrated by the following experiments:—

(1) *Trauma to the denervated limb.*—Cannon and Bayliss showed that trauma to a limb was followed by shock, despite preliminary section of the femoral and sciatic nerves. Simonart repeated this experiment with certain modifications and found that shock failed to develop. We repeated and confirmed Simonart's findings (fig. 14).

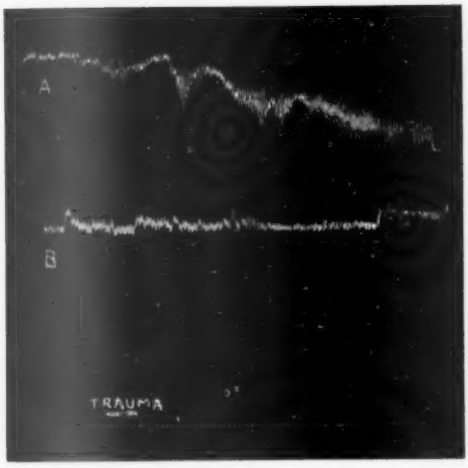
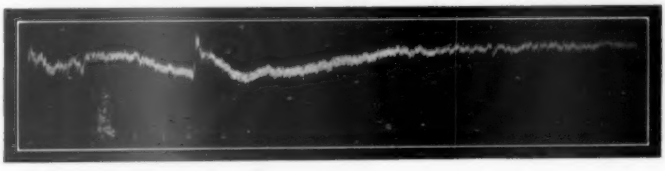
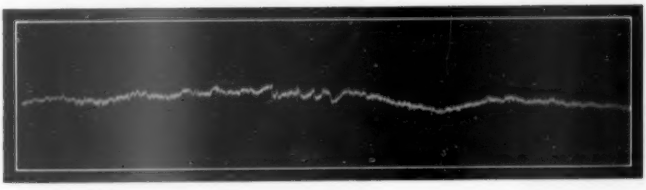


FIG. 13B.—Tracings obtained in experiment illustrated in fig. 13A. Signal 1: Trauma to limb of animal A, supplied with blood from animal B.
Blood-pressure of A falls and animal dies. Animal B only slightly affected.



A



B

C

FIG. 14.—Section of femoral, sciatic, and obturator nerves: Trauma. Cat 99. 3,000 grm. Chloralose. Tracheotomy. Section of femoral, sciatic, and obturator nerves. Blood-pressure 135 mm. of Hg. A, Signal 1: Clip on external iliac artery. Signal 2: Clip off external iliac artery. Signal 3: Clip on external iliac artery. Signal 4: Trauma. Signal 5: Clip off external iliac artery. B, The record three hours after trauma. C, Five and a half hours after trauma. Blood-pressure 125. Animal killed. Increase in weight of traumatized limb 40 grm. Time signal 30 seconds.

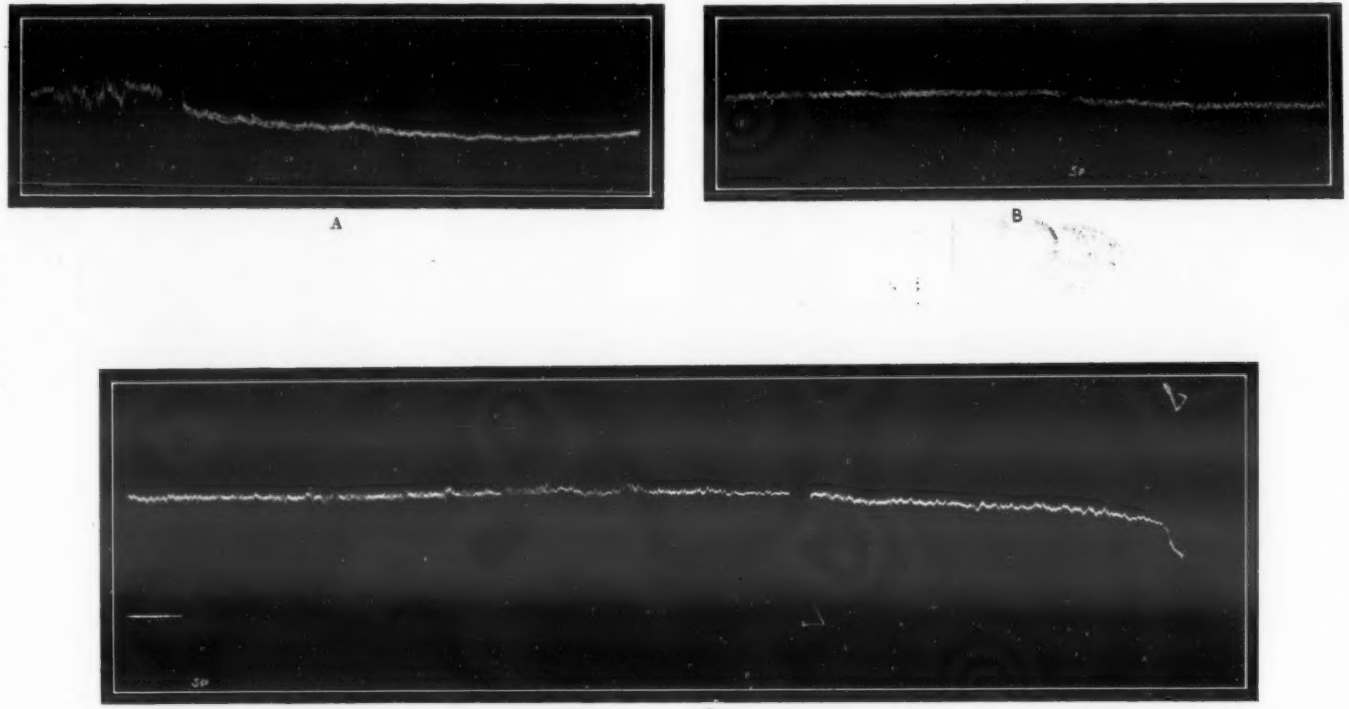


FIG. 15.—Spinal anæsthesia followed by trauma. Cat 17. 3,000 grm. Chloralose. Tracheotomy. A, 5 mgm. novocain in 0·15 c.c. water injected intrathecally, L 4-5. Blood-pressure 150. Spinal anæsthesia maintained by injection every 30 minutes. B, Portion of record four hours after trauma. C, Signal Sp.: Final intrathecal injection. Death nine hours after trauma. Increase in weight of traumatized limb 123 grm. Time signal 30 seconds.

(2) *Effect of spinal anæsthesia.*—When trauma was applied to the limb of an animal kept under continuous spinal anæsthesia, the consequent effect on the blood-pressure was only slight (figs. 15 and 16, and Table II).

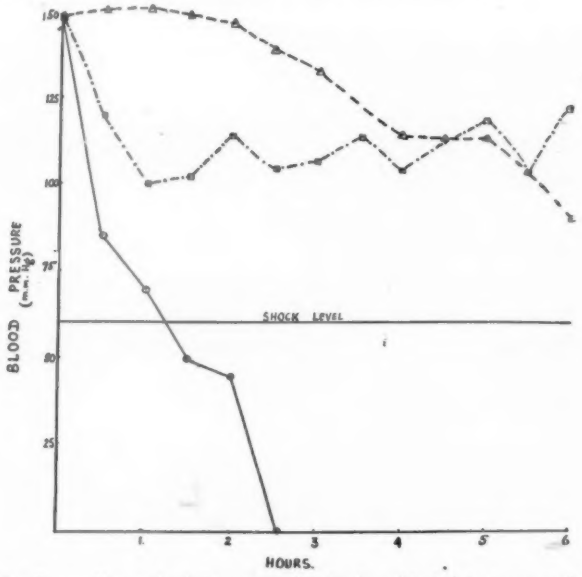


FIG. 16.—Composite graph of the course of animals subjected to trauma of the thigh. Control: ———. Trauma preceded by spinal anæsthesia: -.-.-. Trauma preceded by ligature of the vessels of the thigh: — — —.

TABLE II.—SPINAL ANÆSTHESIA FOLLOWED BY TRAUMA

Cat No.	Weight of cat	Increase in weight of traumatized limb	Fluid loss expressed as a percentage of calculated blood-volume	Initial blood-pressure	Result
	Grm.	Grm.		mm.Hg.	
39	2,000	—	—	170	Killed after 4 hours. B.P. 145
18	2,250	35	20%	175	Killed after 3 hours. B.P. 120
17	3,000	123	53%	160	B.P. after 9 hours, 125. Died after 10 hours
49	3,000	69	25%	120	Died after 8½ hours. (Overdose of anæsthetic)
53	3,800	—	—	165	Killed after 4 hours. B.P. 120
54	4,000	89	29%	180	B.P. after 4 hours, 100. Died after 9 hours
61	4,000	55	16%	170	B.P. after 3 hours, 130. Died after 4 hours. (Overdose of anæsthetic)
16	4,500	—	—	140	Killed after 6½ hours. B.P. 170
46	3,250	—	—	170	Killed after 6 hours. B.P. 140

These experiments are open to the objection that although spinal anæsthesia interrupts nervous pathways, both somatic and sympathetic, it has other effects on the vascular system, and it may be that these are the basis of this beneficial effect.

Presumptive evidence for the nervous factor is provided by the known production of injury-currents in damaged nerves. One thing lacking for complete proof is whether, in fact, nerve impulses passing from the traumatized area to the central

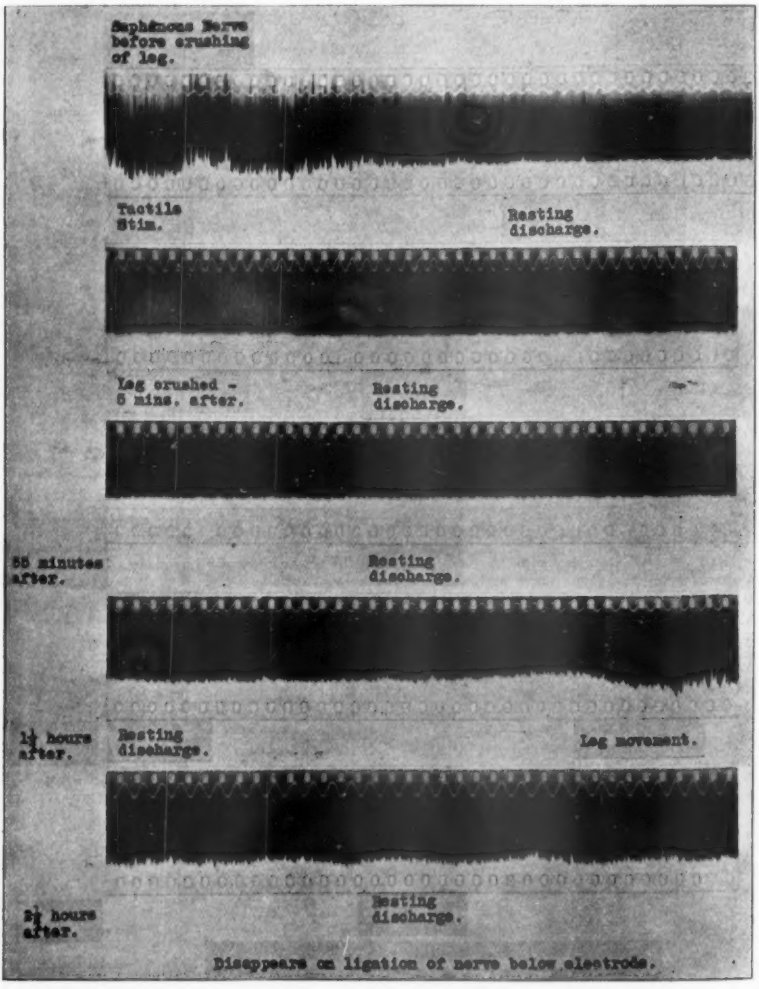


FIG. 17.—Record of nerve impulses from area of trauma.

nervous system can be demonstrated. Direct proof of the existence of such impulses is provided by the following experiment. This experiment was carried out by Dr. Brown of the National Institute for Medical Research, by the kind permission of Sir Henry Dale.

This is a record of nerve impulses from a branch of the femoral nerve (fig. 17). The uppermost portion shows the normal resting discharge, and on the left a discharge of tactile impulses on touching the toes. The limb was then traumatized and records were taken at intervals after trauma. The gradual development of a discharge of centripetal nervous impulses after trauma can be seen.

This finding reinforces in a striking manner the conclusion that the nervous factor is an important ancillary agent in the ætiology of traumatic shock, reinforcing the effects of fluid loss at the site of trauma.

Sir Henry Dale: The experimental basis for the conception of traumatic shock, as a toxæmia due to products released from the injured tissues, was provided chiefly by experiments made during the war by the late Sir William Bayliss and Professor Cannon of Harvard Medical School. Recent experiments of the same kind, but employing more critical methods, have failed to confirm the interpretation which Bayliss and Cannon applied to their results. Mr. Holt and Dr. Slome have added to this critical series, and have given strong reasons for concluding that a traumatic toxæmia plays no significant part in the circulatory depression following an experimental injury of the type used by Bayliss and Cannon, and that the result can be explained by such factors as loss of blood into the injured tissues, which Mr. Holt regards as adequate by itself, or by sensory impulses from the injured area, to which Dr. Slome attaches more importance—on the basis of his experiments with Mr. O'Shaughnessy. It seems to me that their evidence, added to that of other investigators, such as M. I. Smith of Washington and Simonart of Louvain, successfully disposes of traumatic toxæmia as the essential cause of the shock-like condition seen in the Bayliss-Cannon type of experiment. I think it may be of some interest, however, to recall the circumstances in which the idea arose.

Early in the war it became urgently important to have clearer ideas of the factors concerned in the production of a condition which the surgeons working at the clearing-stations had come to recognize as "secondary wound shock." A Committee was hastily constituted by the Medical Research Committee, from a small group of physiologists in London, working in intimate coöperation, for interchange of information and experience, with surgeons working at the front in France. Their primary object was to obtain what information they could from the surgeons dealing with the practical problem, in order to form an idea of the nature of the condition, or conditions, concerning which they were asked to advise.

Experimental work, largely in America, had produced two rival conceptions of the physiological error responsible for circulatory collapse, namely: (1) That it was due to exhaustion of the vasomotor centre by over-stimulation; and (2) that the vasomotor centre was over-active, but failed to maintain an adequate circulation on account of oligæmia—a lack of blood in effective currency. Such evidence as could be obtained from observation under war conditions suggested that the second conception fitted the majority of cases to which the term "secondary wound shock" was applied. Hæmorrhage or sepsis—both of which were usually present to an unknown extent—could obviously bring about such a condition.

Now such a condition could obviously be produced in different ways. Hæmorrhage was the first and most obvious one, and, under the conditions of obtaining the data, it was not possible, in any case, to get an accurate estimate of its extent. Lack of fluids during a long and exhausting transport was another, and the possibility suggested a useful point in prophylaxis. The surgeons, however, were convinced that there were cases in which such factors were inadequate, and evidence was sought for the passage of blood out of currency, apart from loss out of the vessels. An oligæmia of this kind, as a cause of a type of shock, had come to our notice, chiefly through the experimental work of F. T. Mann, of the Mayo Clinic, who had produced it in dogs by prolonged manipulation of the bowels under

anæsthesia. There was only one possibility to account for this passage of blood out of currency, without loss from the vessels, and this was its accumulation in dilated capillaries, where it would become concentrated by loss of plasma into the tissues. Observations made by Professor Cannon while he was still in France, and by other officers, appeared to show that, in the superficial capillaries, there was such a relative concentration of the blood, as compared with that in active circulation, in cases which were regarded as "secondary shock."

Here, then, was the problem defined for us as accurately as it could be under the conditions. Could we suggest any additional factor or factors which could produce such a condition, and indicate any steps likely to prevent it, or to relieve it when it had appeared? A reduction of the alkali-reserve in the blood for a time found favour, especially with Professor Cannon, but we were able to decide by experiment that this could not be a cause, but was only an effect, of the circulatory depression. With Richards, of Philadelphia, and with Laidlaw, I had resumed the study of the action of histamine, and this presented us with a substance which would produce an oligæmic collapse of the circulation, of a type which seemed to have a general resemblance to some of the conditions which were described to us. The action was essentially due to a general loss of tone of the minute vessels, especially of the capillaries, with loss of a large part of the plasma into the tissues, and stagnation in capillary areas of a large portion of the already reduced volume of available blood. This action of histamine served, indeed, to bring, for the first time, to clear recognition the existence of a tone of the capillary vessels and the importance of its maintenance for an efficient circulation. In the cases coming under observation in France, hæmorrhage of unknown amount had usually occurred, and sepsis could practically never be excluded. They were cases in which the primary shock from the injury had long passed away, and in which a secondary condition, presenting the picture of a progressive oligæmia—from whatever complication of causes—had supervened after a long interval. And since a purely toxic oligæmia, such as histamine produced, could be relieved by blood, or gum-saline, transfusion if taken early enough, and since anæsthesia with chloroform or ether was almost a condition of its experimental production, while nitrous oxide had no such contributory effect, its study could at least give some practical hints to the surgeon dealing with secondary shock, whatever the relation between the two conditions.

With regard to a possible rôle of histamine, we know now, what we did not know then, that of all the major tissues of the body, the muscles contain least of that substance.

Whatever else it may have been, the shock following the Bayliss-Cannon limb trauma was not histamine poisoning. Mr. Holt has said that it could be explained by loss of blood and fluid into the site of the trauma, but I cannot explain the whole course of events in that way. There is sufficient loss of blood into the traumatized area to result in a sudden fall of blood-pressure, but hæmorrhage or mere loss of fluid as such into the traumatized area is inadequate as a complete explanation. Dr. Slome has put forward the view that his experiments with spinal anæsthesia demonstrate that an equally important factor is that of the nerve impulses, presumably of a painful type, from the traumatized area, coming up in a continuous series and reaching the central nervous system. That might be the beginning of an explanation, but I do not think these two explanations together represent the whole of it. The shock that was produced was on an animal deeply anæsthetized. I am not sure that it is right to compare that with the shock seen in a street-accident case. To say "sensory impulses" is only to make a preliminary shot at the explanation; it does not describe what has happened. What is it that the sensory impulses do? Is this a return to the vasomotor-exhaustion theory? That would be incompatible with Mr. Holt's evidence, because he, with Macdonald, has put forward experiments in which they showed that in neurogenic shock the blood-volume restored itself by

taking up fluid from the tissues. I agree that arterial dilatation leads to a big fall in blood-pressure, but not to oligæmia—rather to an increase in the blood-volume, because the blood takes up fluid from the tissues. But in his traumatic-shock experiments Mr. Holt has demonstrated that the blood is concentrated and goes on falling in volume as the fatal issue is approached. There is actually an increase in the proportion of blood corpuscles, in spite of the big hæmorrhage. That means that something very different from arterial dilatation has been going on. It is exactly the phenomenon which can be brought about by an overdose of histamine, yet these animals were certainly not suffering from histamine shock. For one thing, histamine shock is a matter of a few minutes, and the shock under investigation here is a matter of hours. I am not at all sure that there has been ruled out the possibility of substances absorbed from the injured tissue, which have a long-range effect and gradually break down the permeability of the capillaries, so that eventually a condition is reached such as has been described. Supposing there are some substances which—not immediately, like histamine, but at long range, with a long latent period in their action—gradually lead to that breakdown of the resistance of the capillary walls: is it not possible that such an effect would come about as the experiments have indicated? In any case I hope that conclusions will not be drawn too widely or too hastily from experiments of one type—trauma of the legs of anæsthetized animals. There are various conditions which have been called shock at different times, and it may be that one of these is here being experimentally reproduced. I do not imagine for a moment that all the conditions are being reproduced, and I do not think that the evidence yet advanced entitles us to rule out some form of toxæmia as an important factor in some kinds of shock.

Mr. Laurence O'Shaughnessy said that he regarded the term "secondary shock" as unnecessary and misleading. It had been introduced in the eighteen-seventies but had soon been abandoned, only to reappear in the literature of the Great War period, when the theory of traumatic toxæmia was also revived.

A state of traumatic shock followed directly on trauma and from this moment the patient experienced no intermission in his symptoms until the syndrome was terminated by recovery or death. Recovery, even from the milder degrees of shock, was only possible after a period to be measured in hours: on the other hand recovery from the sudden circulatory collapse commonly described as a faint was instantaneous.

The subject of traumatic shock was very sensitive to hæmorrhage, and this was the case even if the trauma itself had failed to cause hæmorrhage. The thigh of a cat was traumatized after ligature of its vessels, and although under these conditions there was no local fluid loss, the animal died after withdrawal of 60 c.c. of blood. A normal animal of the same weight compensated quite readily for an external hæmorrhage of this amount.

Mr. Hope Carlton said he spoke, not because he was in any way competent to elucidate the subject, but because it had been said that those with opportunities of making clinical observations did not put them on record.

There were two conditions which presented a clinical picture of so-called secondary shock. One was the acute intestinal intoxication of infants; the other was the late shock of burns, coming on about thirty-six hours after the initial injury, and rarely seen in recent years since tannic acid treatment had been practised.

In both these conditions the blood-vessels were collapsed. At the Hospital for Sick Children, Toronto, both conditions, for a period of one year, were treated by exsanguinating transfusions. The aim was to remove blood from one vein and simultaneously introduce fresh blood into another, so effecting an exchange of most of the patient's blood. The assumption was that such secondary shock was due to

toxæmia by histamines or other toxins. Such treatment would eliminate the toxins. About fifty patients were thus treated under his (the speaker's) observation and the results were critically considered by a surgical committee. The method was abandoned as of little value. It would appear, then, that the premise of toxæmia was incorrect.

Dr. H. E. D. Gale said that Dr. A. G. M. Weddell and himself had made observations on the level of the blood-sugar in patients undergoing surgical operations. The blood-sugar level in all cases had been raised, the extent depending on the severity of the operation and its proximity to the solar plexus. Those operations taking place nearer to the solar plexus had produced a larger rise than those placed nearer to the periphery. In severe cases the blood-sugar was above 200 mgm. glucose per cent., and was found to be still raised twenty-four hours after the operation, when the clinical state of the patient was bad, i.e. the more severely shocked was the patient after the operation, the higher was the level of the blood-sugar and the longer it remained high after the operation.

Section of Urology

President—J. B. MACALPINE, F.R.C.S.

[*May* 23, 1935]

Renal Sympathectomy: Its Scope and Limitations

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ABSTRACT.—(1) Indications for renal sympathectomy, which are deemed to be warrantable by our present state of knowledge.

(2) A disease syndrome is described in detail under the title of "renal sympathetico-tonus."

(3) This is an obstructive nephropathy in which the neuromuscular dysfunction causing the faulty drainage is typically unilateral and due presumably to overactivity of the sympathetic nerve supply to the kidney.

(4) The outstanding features are unilateral renal stasis, renal pain and costo-vertebral tenderness, their recurrence after temporary relief by eserine, and the absence of any demonstrable cause of organic obstruction.

(5) Three stages, which are readily demonstrable by pyelographic methods, are described, namely, (*a*) the stage of irritability or systole, (*b*) the stage of diastole or exhaustion, and (*c*) the stage of paralysis or hydronephrosis.

(6) Immediate and permanent relief of symptoms is afforded by renal sympathectomy in stages (*a*) and (*b*).

(7) In stage (*c*) the aid of plastic surgery may be necessary to overcome secondary organic obstruction.

(8) The best interests of surgery in general and of renal sympathectomy in particular will be conserved by rigidly confining the operation to the type of case described.

RÉSUMÉ.—(1) Indications pour la sympathectomie rénale paraissant justifiées par nos connaissances actuelles.

(2) Description détaillée d'un syndrome, appelé "sympathicotonie rénale."

(3) Cette affection est une néphropathie obstructive dans laquelle la dysfonction neuro-musculaire qui produit le défaut de drainage est typiquement unilatérale, et provient probablement d'une activité exagérée de l'innervation sympathique du rein.

(4) Les caractères saillants de l'affection sont une stase rénale unilatérale, des douleurs rénales et de la sensibilité costo-vertébrale, le retour de ces symptomes après le soulagement temporaire qui suit l'emploi de l'éserine, et l'absence de toute cause organique apparente d'obstruction rénale.

(5) Description de trois stages, facilement démontrables par les méthodes pyélographiques : (*a*) stage d'irritabilité, ou systole, (*b*) stage d'épuisement, ou diastole, et (*c*) stage de paralysie, ou hydronéphrose.

(6) Un soulagement immédiat et permanent des symptomes est obtenu par la sympathectomie rénale pendant les deux premiers stages.

(7) Dans le troisième stage une opération plastique peut être nécessaire pour surmonter une obstruction organique secondaire.

(8) Les intérêts de la chirurgie en général et de la sympathectomie rénale en particulier seront le mieux servis si cette opération est réservée exclusivement au syndrome décrit ici.

ZUSAMMENFASSUNG: (1) Die nach dem heutigen Stand unserer Kenntnisse begründet erscheinenden Indikationen der Nierensympathektomie.

(2) Ausführliche Beschreibung eines Krankheitsbildes unter dem Namen "renale Sympathikotonie."

(3) Hierunter wird eine mit Abflussbehinderung einhergehende Nephropathie verstanden, für welche charakteristisch ist, dass in typischen Fällen die die Abflussbehinderung verursachende neuromuskuläre Dysfunktion einseitig auftritt und vermutlich durch Hyperfunktion der sympathischen Niereninnervation bedingt ist.

(4) Die hauptsächlichsten Erscheinungen der Krankheit sind einseitige Nierenstase, Nierenschmerz, kostovertebrale Druckempfindlichkeit, die sich durch Eserin vorübergehend zum Verschwinden bringen lässt, und das Fehlen jeglicher nachweisbarer organischer Ursache der Stauung.

(5) Es werden drei Stadien beschrieben, die sich leicht durch pyelographische Methoden nachweisen lassen. (*a*) Stadium der Reizbarkeit oder Systole, (*b*) Stadium der Erschöpfung, oder Diastole, (*c*) Stadium der Lähmung oder Hydronephrose.

(6) Sofortige und dauernde Beseitigung der Symptome wird durch renale Sympathektomie in den zwei ersten Stadien erzielt.

(7) In dem dritten Stadium kann eine plastische Operation notwendig werden, um eine sekundäre organische Obstruktion zu beseitigen.

(8) Die Vorteile eines chirurgischen Eingriffes im allgemeinen und der renalen Sympathektomie im besonderen werden am besten dadurch gewährleistet dass man ein operatives Vorgehen streng auf die Art der oben beschriebenen Fälle beschränkt.

WITH us in the Lewisham Hospital, Sydney [1, 2], the operation has been strictly limited in its field of application, and has in no case been employed in conjunction with nephropexy or decapsulation, as practised and recorded by Papin and Ambard [3]. It has been carried out solely for the relief of the pain of increased intrarenal tension, in cases of urinary stasis arising from neuromuscular dysfunction of the renal pelvis, calices and uretero-pelvic junction—a definite type of obstructive nephropathy to which nearly six years ago I affixed the title of "renal sympathetico-tonus."

PHYSIOLOGY

The pelvis and calices constitute a hollow muscular viscus, the rhythmical movements of which are, as in other hollow viscera, subject to nervous influence. The normal sequence is for the calices to contract in regular order from above downwards, followed by contraction of the renal pelvis; the renal pelvis institutes a peristaltic wave in the ureter, which in turn is propagated into the bladder. The terms "systole" and "diastole" have been borrowed to designate the alternate periods of contraction and relaxation which characterize the movements of the renal pelvis. The visualization of these movements by pyeloscopy (which is carried out in our Department as a routine in all patients submitted to pyelography) originally made possible the recognition of the different stages of renal sympathetico-tonus. More recently serial radiography has afforded a most striking method of permanent record. However, a diagnosis sufficient for routine purposes may in most cases be made by pyelography alone, provided that a radiological estimate be made, at the same sitting, of the emptying-time of the renal pelvis.

Delayed emptying-time, or stasis of the renal pelvis.—After pyelography has been carried out, the normal rate of emptying of the renal pelvis, when a watery opaque medium has been employed, may, as Legueu [4] has pointed out, be regarded as approximately 1 c.c. per minute. So that if 10 c.c. have been injected, ten minutes after removal of the catheter there should be little or no evidence of any opaque medium in the radiogram. Any outlining of the pelvis or calices at this time may be regarded as evidence of retention. The denser the shadow, of course, the greater

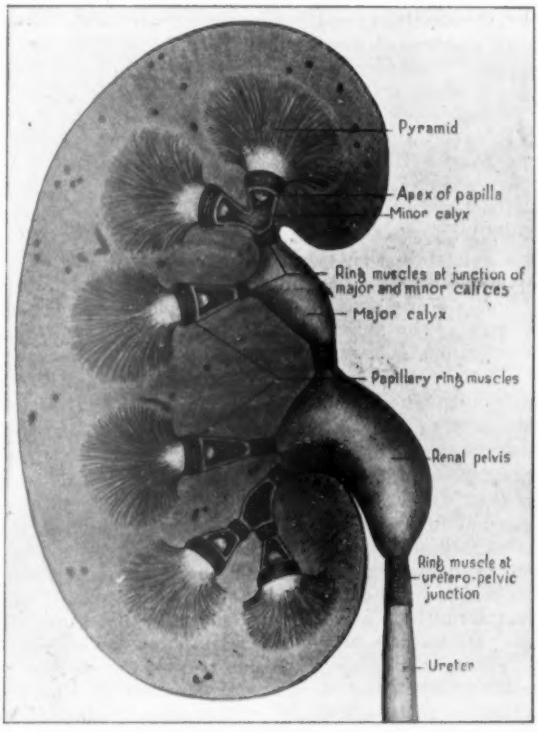

FIG. 1.—Diagrammatic representation of the ring-muscle system of the renal pelvis and calices described by Kelly and Burnam. The anterior wall of each minor calyx is here shown cut away to expose the enclosed papilla. It will be seen that a ring-muscle surrounds the base of each papilla, the junction of each minor and major calyx and the uretero-pelvic junction. The ring-muscle in the latter position is the strongest of the group. The ring-muscles are shown much enlarged for purposes of illustration.
(Elaborated from the original in Kelly and Burnam, "Diseases of Kidneys, Ureters and Bladder.")

the stasis or delay in emptying-time. Stasis, we have found, may and, not infrequently, does occur in a pelvis of normal size.

Ring-muscle system of the kidney.—The muscular system of the renal pelvis and calices includes, in addition to the longitudinal and circular muscle-fibres appertaining to them as components of a hollow viscus, the ring-muscle system described by Kelly and Burnam [5] (fig. 1). The later work of Muschat [6] provides con-

firmation of the original findings of these authors, so far as the papillary ring-muscles are concerned. The evidence afforded by pyeloscopy, if not completely confirmatory, is at least extremely suggestive of the accuracy of the description by these authors of the ring-muscle system of the calices and pelvis.

Ætiology of renal sympatheticotonus.—Of the ætiological factors concerned, little or nothing definite is known. The disease rarely attacks people in robust health. Worry and overwork have been outstanding features in nearly all cases. The attacks of pain are believed to be brought about by increased excitability of the sympathetic nerve supply to the kidneys, possibly due to vaso-constriction of the spinal cord (Royle), though this sympathetic over-activity, while commonly unilateral, may often be shown to be much more comprehensive in its distribution. Evidence of this is to be found in muscular hypertonus, illustrated in this series of investigations by increased excitability of the knee-jerk on the affected as compared with the normal side with delayed relaxation time and absence of the normal oscillations. Hypertonus, as estimated by the knee-jerk, is liable to variation from time to time in the same patient, and is subject at the time of examination to the phenomenon of "fatigue." The latter is quite an important consideration. For this reason attention should be focused on the first tests made, and the patient should be properly prepared by removal of boots.

It is reasonable to suppose that this periodical variation of hypertonicity applies also to the kidney, affecting the entire musculature. The intermittent nature of the pain would thus find a ready explanation. The renal stasis, as exemplified by the delayed emptying time of the renal pelvis after pyelography is, however, a constant finding, and if once present is always present until relieved by eserine injection or operation.

Stages of renal sympatheticotonus.—The disease tends to fall naturally into three stages, which pass, more or less insensibly, one into another.

(1) The stage of irritability or systole: In this first stage of renal sympatheticotonus the condition of systole or contraction of the renal pelvis and calices predominates, so that, from pyelography, the pelvis and calices of the involved kidney, though normal in outline, may appear actually smaller than those of its normal fellow. Delayed emptying time, however, as stated above, is a constant feature. This stage is characterized by frequent, irregular and inefficient contractions of the calices and pelvis, many of which are not transmitted. The pain, as a rule, during attacks, is intermittent and colicky, and generally, though not necessarily, moderately severe. Hæmaturia may be an outstanding, but rarely the only feature. I have seen four examples of this. The constriction of the base of a papilla by a spastic ring-muscle would afford a ready explanation of this phenomenon. A hypodermic injection of eserine (gr. $\frac{1}{60}$) will induce, within 15 seconds, regular powerful contractions of the pelvis and calices with rapid emptying and relief of pain. This is a diagnostic sign of considerable value, since in cases of organic obstruction the increased intra-pelvic tension brought about by eserine will either accentuate the pain—or, possibly, induce it, if it is not present at the time.

The irritability of the pelvis, which characterizes this stage of the disease, probably varies from time to time in the same patient (*vide supra*) and may even, particularly during an interval period, be absent at the time of examination. The delayed emptying-time, as stated is, however, a constant feature, and in conjunction with the other symptoms is sufficient to determine the diagnosis.

(2) The stage of exhaustion or diastole: Here the relaxation of the renal pelvis and calices predominates, even during interval examination, so that the pelvis and calices will appear larger than those of the opposite side even when little or no actual dilatation or clubbing of the calices has occurred. The flabby, atonic

diastolic pelvis (*see* fig. 2) presents a striking picture in serial intravenous urography. Pyeloscopy demonstrates irregularity and inefficiency of the contractions, which are generally infrequent and powerful.

This stage is characterized by more prolonged periods of dull pain or discomfort in the loin, with periodical acute exacerbations. The emptying of the renal pelvis, estimated by pyelography, is completely held up. A hypodermic injection of eserine has the same effect as in Stage 1, and will generally serve to differentiate with certainty this stage of the disease from the obstruction caused by aberrant vessels or organic stricture at the uretero-pelvic junction, which examination of the

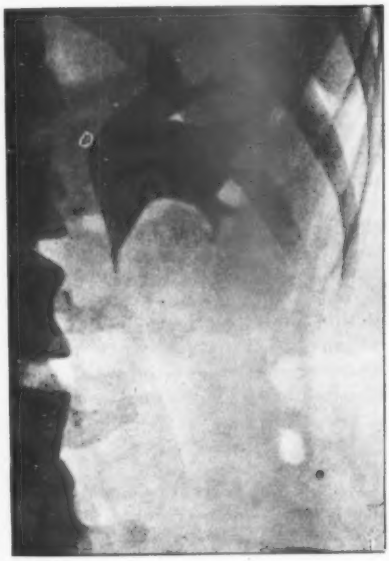

FIG. 2.

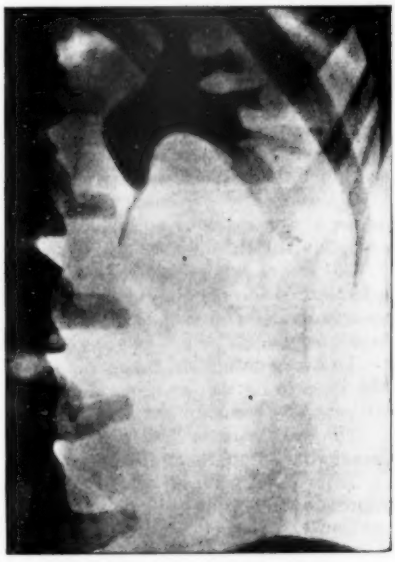

FIG. 3.

FIG. 2.—Intravenous urogram illustrating Stage 2 of renal sympatheticotonus before renal sympathectomy. Pelvis diastolic, with perhaps slight dilatation; slight broadening of the calices. Serial radiography at this time showed the renal pelvis to be in a condition of more or less persistent diastole.

FIG. 3.—Intravenous urogram, same case as fig. 2, after renal sympathectomy. The diminution, illustrated here, in the size of the renal pelvis was fully confirmed by the serial radiograms.

pyelograms alone might justifiably suggest. Any clubbing of the calices and dilatation of the pelvis disappear more or less completely after sympathectomy (*see* fig. 3).

(3) The stage of dilatation or paralysis: In this, the third stage, any grade of hydronephrosis may be present. This is the stage of retention with overflow and is comparable to Hirschsprung's disease of the large bowel. It is associated with relative immobility of the pelvis and calices and is characterized by infrequent attacks of renal pain, generally of great severity. The pain is relieved by a hypodermic injection of eserine unless organic obstruction is also present. Some of the cases of bilateral hydronephrosis, in which there is neither ureteral dilatation nor

primary obstruction at the uretero-pelvic junction, are almost certainly examples of this stage of renal sympatheticotonus.

Some Special Features

A valuable test which may be carried out on the operating-table, either before or after sympathectomy, is the reaction to a hypodermic injection of eserine, which will induce regular and powerful contractions unless organic obstruction is present at the uretero-pelvic junction. The presence of organic obstruction, which may be of the nature of valve formation or of congenital or acquired stricture, will prevent normal contraction and will, of course, be a very definite indication for exploration of the uretero-pelvic junction. When plastic repair of hydronephrosis has been undertaken and no definite organic cause of obstruction has been discoverable, it would be sound practice to complete the operation by carrying out a renal sympathectomy. Some of the disappointments which occur after the apparently successful repair of hydronephrosis will thus be avoided.

Distension of the renal pelvis in renal sympatheticotonus is never so "tight" as that sometimes found in organic obstruction alone and, as stated, will react to eserine unless it is complicated by organic obstruction.

All stages of the disease are characterized by tenderness in the costovertebral angle, at any rate during a painful period, generally by normal urinary findings and, except in the third stage, by little or no interference with the renal function.

All stages are liable to be complicated by attacks of so-called "pyelitis," due to infection of the residual urine. This sometimes, especially in the third stage, leads to organic deformity of the uretero-pelvic junction and upper part of the ureter due to adhesions. The pre-existing stasis is thereby aggravated.

In every patient in Stage 1 or 2, who has come under observation, the renal pain has been unilateral and, in the absence of infection, localized to the renal area and without any concomitant bladder disturbances.

In two patients the disease later manifested itself in the opposite kidney, demanding sympathectomy.

After renal sympathectomy in Stages 1 and 2, the renal pelvis and calices resume approximately their normal function and little evidence can be found of any previously existing dilatation or stasis (*see* figs. 2 and 3). In Stage 3, however, even after a successful sympathectomy, the pelvis and calices remain permanently dilated. The emptying time, though markedly improved, in advanced cases at any rate, remains permanently impaired, and there is always some residual urine in the pelvis and calices. This may be further improved in suitable cases by some type of plastic operation on the renal pelvis.

Diagnosis of renal sympatheticotonus.—For practical purposes the outstanding diagnostic features of renal sympatheticotonus may be summarized briefly as follows: (1) Renal pain and costo-vertebral tenderness, confined to one side only, (2) the recurrence of pain after its immediate, though temporary, relief by eserine, (3) urinary stasis, proved by urography, localized to the pelvis and calices of the affected kidney, (4) less frequently, the hypertonic knee-jerk on the side of the lesion, and (5) the absence of any demonstrable cause of organic obstruction.

In the majority of cases of renal sympatheticotonus the diagnosis is clear-cut and leaves no room for doubt. Occasionally the absence of organic obstruction at the uretero-pelvic junction will, notwithstanding the most thorough investigation, have to await final verification at the time of operation. In the third stage, when there may have developed a secondary organic obstruction at the uretero-pelvic junction, the primary lesion may very easily be overlooked. Much research still remains to be done.

Operative Technique

The performance of a complete operation is necessary to ensure permanent success. Adequate exposure and illumination of the field of operation are essential, the operation is otherwise quite impossible.

The original technique of Papin [7] by which the fatty tissues are gradually wiped back in a mesial direction with gauze from the vessels of the renal pedicle is fraught with grave risk of hæmorrhage from tearing of the renal vein or its

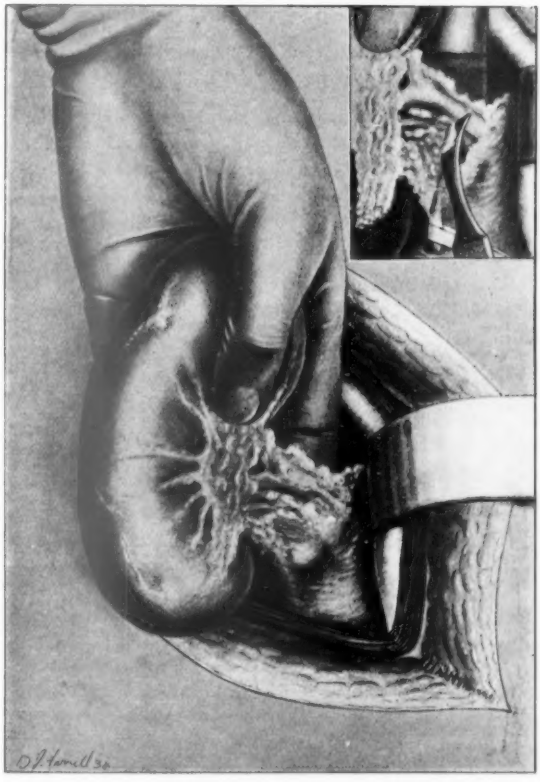

Fig. 4.—Renal sympathectomy, illustrating the author's method of exposure and finger-point control of the vessels of the pedicle. *Inset* shows method of instrumental dissection; anterior surface of vein completely cleaned up; dissection of artery just begun.

branches, and this hæmorrhage may be difficult to control or may even demand nephrectomy. The author and his brother, Dr. R. G. Harris, used this method in their earliest cases and twice had to carry out nephrectomy to control the bleeding. This technique was soon abandoned and the method described below was substituted. The kidney is exposed extra-peritoneally through a boomerang-shaped lumbar incision, and completely delivered from its fascial and fatty coverings.

Beginning as far away from the kidney as is reasonably possible, the pedicle is isolated from the surrounding tissues, the operator working continuously outwards towards the kidney. It considerably simplifies the operation when the pedicle can be approached at some distance from the kidney, before the vessels begin to branch. When the kidney can be completely delivered this is a comparatively easy matter, but in the presence of a very short pedicle it may be impossible, and the dissection will have to begin closer to the hilum of the kidney and be carried out in the depths of the operative field.

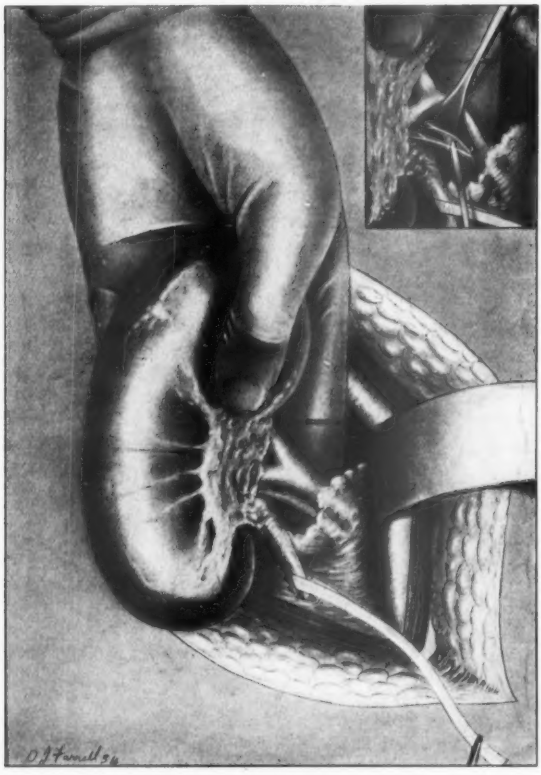

FIG. 5.—Renal sympathectomy, showing completed operation. Renal artery and vein, renal pelvis, uretero-pelvic junction and upper portion of ureter completely cleaned up. *Inset* indicates method of denervation of renal artery.

After the pedicle has been isolated the individual vessels are attacked in turn by careful instrumental dissection, a beginning being made on whichever aspect of the pedicle affords the more ready access and the surgeon always working in the direction of the kidney. Each vessel is carefully denuded of connective tissue and all the tissue lying between the vessels is removed. *The vessels of the pedicle, throughout the dissection, are supported and rendered prominent by the fingers of the left hand placed behind them* (*see* figs. 4 and 5). The pedicle is thus, at all times and in all

situations, under the immediate control of the operator and any bleeding vessels are easily controlled by increasing the forward thrust of the underlying fingers and are picked up at leisure by fine-pointed forceps and tied. Fine silk should be used in this situation, in preference to catgut; it can be tied more firmly and is not so liable to slip or be wiped off.

After a complete operation, in addition to a careful denudation of the renal artery or its main branches, and of the renal vein, the renal pelvis on both aspects as far as the hilum, the uretero-pelvic junction, and the first inch of the ureter will also have been cleaned up, the superior ureteral nerve being divided in the process. Finally the kidney will be attached solely by its denuded vessels and ureter (*see* fig. 5).

The increased safety and operative facility which are attained by keeping the fingers of the left hand at all times in contact with the reverse side of the pedicle to that on which the operator is working cannot be too strongly emphasized. A tear even of the renal vein may thus be ligatured with striking simplicity. Of this the author has had more than one experience.

A hypodermic injection of eserine should be given at the end of the sympathectomy and will be followed within fifteen seconds by strong peristaltic contractions of the pelvis and ureter. This is a useful indication that all is clear in the pelvi-ureteral excretory apparatus. In cases of organic ureteral obstruction eserine may either have no visible effect, or may cause fibrillary contractions of the pelvis. The contractions return to normal only when the obstruction is removed. These phenomena the author has actually observed several times on the operating-table, and also in the laboratory animal.

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Mr. C. A. Wells: I have performed the operation of renal sympathectomy on about twenty occasions, but, unlike Mr. Harris, always in conjunction with some other procedure. Thus, of the twenty, I have done a nephropexy in every case and also performed a plastic operation for hydronephrosis in two. In one of these two a stone was present in addition to the hydronephrosis, and in another case of hydronephrosis there was a stone which was removed, although the treatment of the primary condition was by sympathectomy only.

My method of selecting cases for operation has differed from that laid down by Mr. Harris in one or two respects, although I think that, in the main, those in which there has been no gross anatomical change necessitating interference are cases which would have been submitted to this operation by him.

Although we have not made use of the method of pyeloscopy and have consequently not made observations upon the effect of eserine, the cases have, none the less, been very fully investigated and in every instance the operation has been undertaken only after a long period of deliberation and after other methods of treatment have been given full trial.

To consider then, first, the cases of manifest abnormality. These consisted of six cases of gross hydronephroses. Of these, three were of a moderate size (fig. 1) and were treated simply by means of sympathectomy and nephropexy. Aberrant

vessels, when found in this group, were not divided as in no case did they seem to be primarily responsible for the trouble. In one of these cases a stone had formed and was removed. All three patients are now completely relieved of their symptoms. Two other cases of hydronephrosis were dealt with by means of sympathectomy and resection of the pelvis by a modification of Thompson-Walker's technique. In one of these, the patient also had a stone. The results in both cases have been entirely satisfactory. The sixth and last hydronephrosis was exceedingly large and was situated on the left side. The only pain complained of was on the right side, where it was reproduced by means of a pyelogram and on which side a pelvis of the "systolic" type, as described by Mr. Harris, was found. In this case I performed a bilateral operation at one sitting. The pain on the right side was completely and

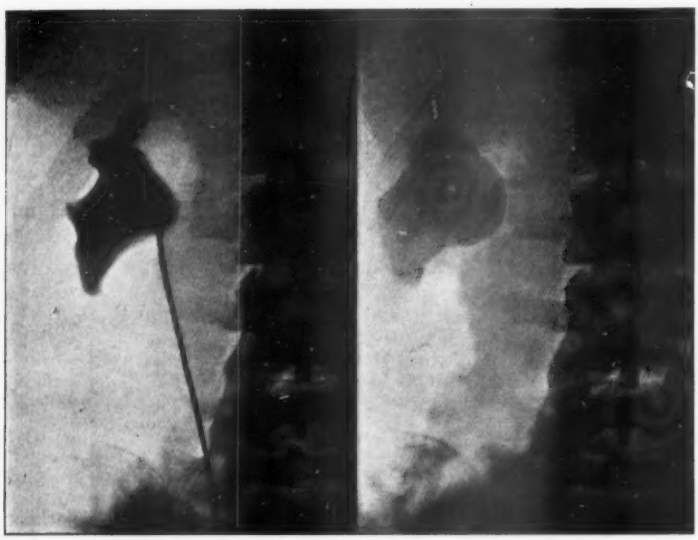


FIG. 1.—Instrumental and intravenous pyelograms in a case of hydronephrosis treated by sympathectomy and nephropexy with complete symptomatic relief.

permanently relieved, but the large hydronephrosis became mildly infected and subsequently increased in size and had to be removed. Incidentally, the bilateral operation caused no ill-effects (fig. 2).

Another case is so unusual as to defy classification. In a woman of 50 there was a complaint of left kidney pain, which was reproduced by means of a retrograde pyelogram. The pelvis was not otherwise abnormal. On the right side there was a stone in the upper calyx of the kidney, but there was no pain. This patient was particularly anxious to avoid multiple operations, and at one sitting I undertook removal of the stone from the right kidney and performed a sympathectomy and nephropexy on the left. Since this date the patient has been free from pain on the left side but complains of pain on the right. Recent investigations disclosed normal function on both sides and absence of any pathological condition on either.

Yet one more case (fig. 3) is unusual, in that the kidney was ectopic and discoid,

FIG. 2.—A case in which simultaneous bilateral sympathectomy was performed for right-sided pain with left hydronephrosis. The hydronephrotic kidney became infected and was subsequently removed. The pain on the right side was relieved from the time of the first operation.

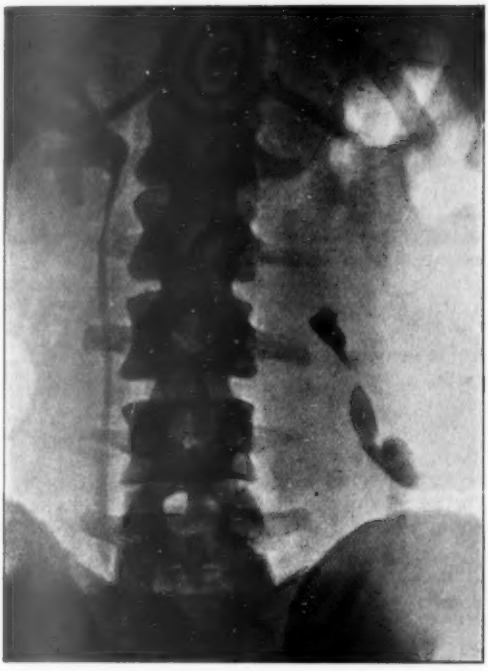


FIG. 3.—An ectopic kidney on which sympathectomy was performed, with relief of pain.

being situated low down on the right side. In all other respects this case resembles the remaining twelve which are about to be described.

These twelve cases all failed to show any gross anatomical abnormality (figs. 4 and 5) and had good function as estimated by urea content, dye-excretion and uroselectan. Some degree of ptosis was present in four, and in three others the angle between the upper end of the ureter and the pelvis was modified in such a way as to constitute what might be fairly described as a very early stage of pelvic hydronephrosis. All the patients were women.

The thirteen last-described cases are of the type in which it has been difficult to decide whether sympathectomy was justifiable. All the patients have complained of a dull aching pain in the costo-vertebral angle, and several have experienced severe exacerbations of a violent, colicky nature, associated with collapse and vomiting. My routine has been to submit each patient to a full general examination and, if necessary, to exclude, by means of special investigations, the likelihood of disease in the gall-bladder, gastro-intestinal tract or pelvis. Following this, a complete investigation of the urinary tract has been undertaken, including microscopic examination and culture of the urine, X-ray examination, uroselectan, dye-excretion in most cases, and finally, retrograde pyelography. All the cases with which we are dealing were free from urinary infection and from evidence of other disease, although many had previously been operated upon for supposed appendicitis, gall-stones or some gynæcological disorder.

As we have placed a good deal of reliance upon the pain-reproduction test, I should like to place some emphasis on the amazing consistency and certainty with which our patients have answered the questions put to them. When the retrograde pyelogram is made they are asked whether the pain which it causes is the same as that of which previously they have complained. In a great majority of cases the reply is quite definite. The patient will either say "No, I have never had a pain like that before," or, "Yes, definitely; only this is much worse" (or, alternatively, "Not so severe"). In the small group of cases in which there is any hesitation we have always assumed the test to have given a negative result. When the result has been positive it has been my practice to send the patient back to her doctor and to advise him to treat her symptomatically and encourage her to believe that with care she would get well. I have, at the same time, indicated to the practitioner that if the symptoms persist for more than from three to six months, it would be worth while to repeat the examination and to consider a sympathectomy. In the earlier days many of these patients disappeared, but it is surprising to find them coming up again now after a period of years, still with a consistent story of complaint, and still showing a positive pain-reproduction test. I have regarded such a train of events as a reliable indication for the operation and in every case except one the results have amply justified that opinion. With this single exception—the patient being an intensely neurotic woman, the subject of general visceroptosis, who still complains of a painful and tender kidney—all the patients have been relieved of their pain, and strikingly grateful for what has been done for them (figs. 6*a* and 6*b*).

The operative technique.—This has not varied from that described by Mr. Harris, except that the use of carbolic acid, as recommended by some other workers, has been found helpful. This is used in 10% solution and is applied to the vessels after the greater part of the fibres have been stripped away. Any remaining fibres rapidly become whitened and can be recognized and removed much more rapidly.

In conclusion I may say that by means of careful and conservative selection we have had in this series of twenty cases a high percentage of entirely successful

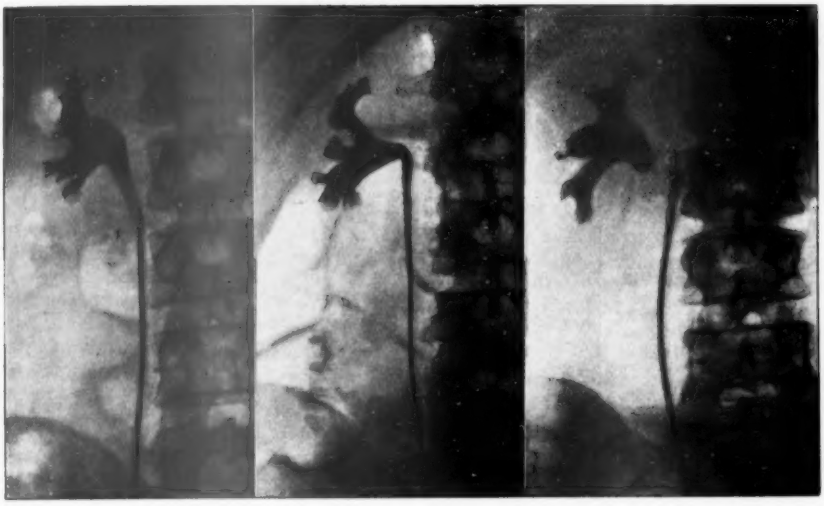


FIG. 4.

FIG. 5.

FIGS. 4 and 5.—Retrograde pyelograms in cases treated for pain, without gross anatomical change, illustrating the types of pelvis found.

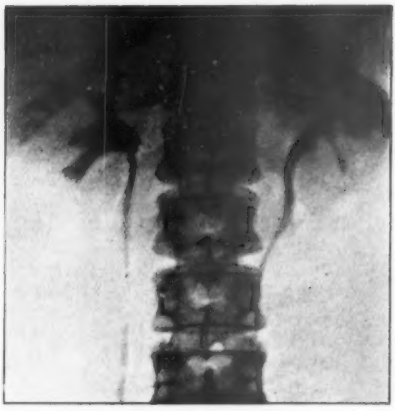


FIG. 6*a*.

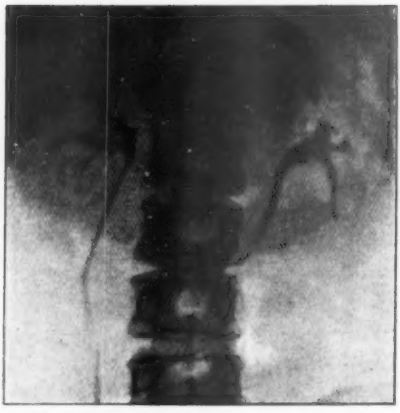


FIG. 6*b*.

FIG. 6*a*.—A small pelvic hydronephrosis treated by sympathectomy and nephropexy. Pain had been of an aching character with exacerbations.

FIG. 6*b*.—The same case eighteen months later. Complete symptomatic relief had been obtained.

results in a group of patients whose outlook might otherwise have been regarded as anything but cheerful. I feel sure that by making intelligent use of the operation and methods of selection described by Mr. Harris, we shall, in future, extend the hope of operative relief to a large number of patients for whom otherwise we should have been able to do little or nothing.

[*June* 14, 1935]

Six Cases of Chronic Retention of Urine in Women caused by Dysectasia of the Bladder Neck

By G. VAN HOUTUM (The Hague)[1]

DURING the last two years my partner, Dr. C. C. A. Croin (*Cases II, IV, V*) and myself (*Cases I, III, VI*) have observed six cases of chronic retention of urine in women, all suffering from a syndrome similar to that of prostatic enlargement. The bladder showed trabeculation more or less pronounced, sometimes saccules. The urethra was neither compressed nor obstructed; all instruments passed easily. The signs of back pressure started at the bladder neck, indicating a difficulty in relaxation. To this condition Legueu has applied the word "dysectasia."

The retention of urine could not be attributed to disease of the central nervous system. In one case there was, however, a spina bifida and another patient suffered from Parkinson's disease.

We have treated all these cases with the cautery-punch of John R. Caulk, and we have obtained either a completely normal condition, or a great improvement.

Case I.—Miss A. S., aged 29, was seen in June 1933 in a uræmic condition, the blood-urea being 1·684 grm. per 1,000. She was suffering from a chronic incomplete retention of urine. The residual urine amounted to more than 1,500 c.c. (three pints). The bladder showed marked trabeculation and saccules. The kidneys and ureters were badly damaged by back pressure with superimposed infection. The dysuria had appeared in early childhood. For the last four years she had been permanently under medical care. So we are quite sure, that all these four years there existed this great amount of residual urine. A spina bifida was found, to which the retention of urine was attributed. An indwelling catheter was inserted for drainage for two months. During this time a slow but steady improvement was made. She felt less thirsty, the appetite improved, she put on flesh, and her blood urea fell to 0·85 grm. per 1,000. The indwelling catheter was then removed and the bladder emptied twice a day. She still improved, but if catheterization was discontinued, the difficulties in urinating and the residual urine recurred.

I decided to carry out an operation on the neck of the bladder with the cautery-punch, as in the treatment of male patients. The sheath was inserted, the obturator was withdrawn, the posterior border of the sphincter was caught in the fenestra and pressed on firmly. Under control of my finger in the vagina I got the impression that there was enough tissue to be punched out, without danger of doing damage, so I withdrew my finger and finished the operation. The result was encouraging, the residual urine fell to 250 c.c. The patient herself was satisfied because the micturition was easier and faster and remained so. After four weeks I carried out another punch and subsequently she emptied her bladder completely after passing water.

Now a year and a half has elapsed. The state of the kidneys and ureters has not improved. Pyelograms show that the ureters are widely dilated and twisted, and the calices and pelves dilated and blunted. The infection has remained. The patient has had three or four attacks of temperature and pain in the loins. I have had to make regular dilatations of the urethra to counteract relapses of dysectasia. An additional punch had to be executed. Sometimes, especially during menstruation, she was more or less incontinent. Her present state, however, is infinitely better than it was before and makes life less difficult to her.

I learned from this case that some types of retention of urine in women may be abolished by a punch operation upon the neck of the bladder, that in female patients a punch is possible, and that with reasonable care damage can be avoided.

[1] Read at a Joint-Meeting with the Dutch Urological Society.

Case II.—Mrs. C. C. M., aged 64, seven children, was seen on August 2, 1934.

For two years she had been suffering from dysuria, viz., frequent urgency, and burning, difficult micturition. During the last two months this disturbance had increased; with the utmost endeavour only she could pass a little water. The abdomen was distended by the bladder which contained nearly 2,000 c.c. (four pints) of urine. She was uræmic (blood urea 1·081 grm. per 1,000) and also suffered from diabetes (4·4% glucose). The bladder showed trabeculation and the sphincter muscle was thickened throughout. The diabetes was controlled by appropriate treatment. The bladder was regularly emptied and washed out. The urethra was dilated. The general condition of the patient improved, the blood urea became normal (0·373 grm. per 1,000). The retention of urine however remained.

Four weeks after her admittance a punch operation was performed, and ten days later the operation was repeated. The amount of residual urine after the first punch fell to 400 c.c. and after the second punch to 60 c.c.

Eight months after the last punch she came to see me. All the troubles of micturition had gone.

Case III.—Mrs. J. M. B., aged 31; no children. From early childhood there were urinary complaints, viz., nocturnal incontinency and frequent urgency in day-time. At school she was allowed to absent herself without asking. After menstruation had set in, her condition changed in a remarkable way. She did not feel any need to urinate, and passed water only once or twice daily. Sometimes, however, urine escaped involuntarily, when she rose suddenly.

During the months of July and August 1934, she had painless hæmaturia on three occasions. For this reason she was advised to see me. After a careful examination of the whole urinary tract, I came to the conclusion that there must have been a hæmorrhage from the congestive and inflamed bladder mucosa.

Unexpectedly I found that the bladder was not emptied in passing water. There remained 300 c.c. of urine. According to the extent of the cystitis, the quantity of residual urine varied from 300 c.c. to 600 c.c. The bladder was trabeculated. The sphincter muscle was thickened, and showed a blunt ridge between the floor of the bladder and the urethra.

The cystitis was treated and the urethra dilated. The patient was urged to try regularly, four or five times daily, to pass water. She improved in so far that the stimulus to urinate returned and the incontinency disappeared. The chronic incomplete retention of urine remained. We decided, therefore, to perform a punch operation, after four months of unsuccessful outdoor treatment.

She was admitted on January 15, 1935, and a punch operation was performed. The operation had to be repeated three times. Each time the residuum diminished. On February 12, she was discharged; the residual urine was still 100 c.c. Observation has been continued during outdoor treatment, and since April 15, there is no residual urine. Micturition is normal.

Case IV.—Mrs. O. d. V., aged 56; two children. Since the extirpation of the uterus, for fibromyomata, ten years ago, she had dysuria. During the last three years it became worse. The micturition was difficult and frequent, the stream irregular, and she was much troubled by incontinence.

She entered a nursing-home on January 14, 1935. The urine was purulent and she had chronic incomplete retention with 600 c.c. of residual urine. Her blood urea had increased to 0·736 grm. per 1,000. After some weeks of indwelling catheter, the general condition had much improved. The blood urea went down to 0·405 grm. per 1,000. The retention of urine remained.

On February 26, the operation of cautery punch was carried out, and on March 22, she went home. There remained a residual urine of 100 c.c. The micturition interval was about every three hours. During the night there was sometimes incontinency, especially after the use of narcotics. There was still a cystitis, and she remained in outdoor treatment. The cystitis was very rebellious; the urinary troubles varied. The quantity of residual urine rose again to 400 c.c.

On May 18, we carried out another punch operation. This time we did it in the out-patient department, and had not to regret this concession to our patient. She is still under treatment; the residual urine has fallen to 250 c.c. Probably another punch operation will be necessary.

Case V.—Miss Z., aged 56. This patient had been operated upon on February 18 of this year, when total hysterectomy was performed for carcinoma cervicis uteri (by Dr. J. de Groot). Complete retention of urine followed. The usual measures were taken, without success, however. A catheter had to be passed twice daily. In the beginning the urine was clear, but later it became infected. Before the operation there had been complaints about frequent urgency and burning, but nothing was known about retention of urine. The bladder showed a slight trabeculation. The demarcation between the floor of the bladder and the urethra was sharply marked. At the roof-side the sphincter was thickened and the ridge irregular. The patient suffered from a cystitis colli.

We tried dilatations of the urethra in vain. After seven weeks of complete retention of urine, we felt justified in trying a punch operation, which we did on April 16. After some days the spontaneous passing of urine was beginning, and ten days later she entirely emptied her bladder. The patient herself was satisfied, because micturition was far better than before the operation. She now micturated four to five times daily, without burning pain. Up to this day she is well.

It is doubtful whether there was chronic retention of urine before the hysterectomy. The post-operative retention was of an unusually stubborn character; we attributed this to the cystitis colli, and were supported in this opinion by the microscopic examination of the punched-out pieces of the sphincter. The slices showed a chronic sclerosing inflammatory process similar to that found in our other cases. In view of this case we would advance the opinion that the punch may become a useful instrument in combating difficult and prolonged post-operative retention of urine.

Case VI.—Mrs. R., aged 73; no children. This patient has been treated for ten years. She came under observation in March 1925, on account of acute cystitis, and had at the same time complete retention of urine. This illness had overtaken her suddenly; formerly she had no urinary troubles. After six weeks of indoor treatment the urine became clear. There, however, remained a chronic incomplete retention, the quantity of residual urine amounting to 250 c.c. An examination by a gynæcologist and a neurologist did not explain the cause of the retention.

For the past ten years the patient has visited me about once a month for supervision and treatment. During these ten years the quantity of residual urine has gradually increased to 1,400 c.c. There is no sign of a serious back-pressure action. The kidneys are not deficient, the blood-urea does not exceed 0·500 grm. per 1,000, and there is never incontinence. The bladder shows marked trabeculation. The sphincter is thickened all round; at the posterior margin there is a distinct ridge of demarcation between the bladder floor and the urethra.

During the ten years there have been some attacks of acute cystitis, and once there was a severe hæmorrhage. For the last eight years she has also suffered from Parkinson's disease.

Encouraged by our successes in cases of retention of urine in females, we proposed to treat her in a similar manner. The punch operation was performed on May 7, 1935. One central and two lateral bites were made. Next day the residual urine had fallen from 1,400 to 500 c.c. A second punch operation had to be performed on May 15. The residual urine is now down to 100 c.c. She passes water five or six times daily; she does not rise during the night.

Punch operations have twice been carried out under general anæsthesia, on account of the extreme nervousness of the patients. As a rule, we have operated under local anæsthesia; an injection of percain (0·3%) or alipin (2%), through the urethra, proved to be satisfactory. We operate in a dry field, on the posterior wall of the sphincter muscle between 4 and 8 o'clock. Generally we make three bites, the first at the most prominent point, the other two at each side of this point. Each bite takes about two seconds.

This operation is done with the intention of allowing the sphincter to regain the degree of flexibility necessary for its function. These operations are more delicate in women than they are in men, so we took due care not to cause irreparable damage, and this may be the reason that we had to repeat the operation.

With the exception of *Case V*, these are all cases of chronic retention of urine in women. In all cases the punch operation has given surprising results.

About two years ago the surgery of the neck of the bladder was discussed at the Fifth Congress of the International Society of Urology (London 1933) but only as carried out in the male.

In the last edition of his textbook on Urology (1934) Wildbolz remarks, that disease of the bladder-neck has never been seen in women. He holds, therefore, that the specific male organs must be in some way connected with this disease.

In the discussion of the reports on the London Congress, a few cases of this disease of the bladder were mentioned to have occurred in women. Jean de Smeth (Brussels) was the only member who stated that it was an omission of the openers to exclude the surgery of the neck of the bladder in female patients. De Smeth[1] published a communication on "The Polyps of the Neck of the Bladder in Women." He recommended treatment of these cases with electro-coagulation. De Smeth considered his cases identical with the cases in which the openers applied surgery to the bladder neck. In the fifteen cases of de Smeth residual urine was only found in three of them. The remaining twelve were cases of cystitis and cystitis colli.

In our cases similar alterations of the neck of the bladder were found, to those which were described by de Smeth. In fact the only difference between cystitis colli and our cases, is the chronic retention of urine.

POSTSCRIPT.—Since completing this communication I have found in the May number of the *Journal of Urology*, a paper by Dr. John R. Caulk and Dr. John F. Patton, on "The Cautery Punch for the Removal of Obstructive Lesions at the Vesical Orifice in Women and Children." Our general ideas are so nearly identical that I need not do more than refer to the publication.

[1] *Bull. de l'Acad. Roy. de Méd. de Belgique*, 1929, p. 262.

Section of Neurology

President—S. A. KINNIER WILSON, M.D.

CLINICAL MEETING, MAY 16, 1935, AT THE NATIONAL HOSPITAL, QUEEN SQUARE, W.C.1.

Peripheral Neuritis and Pernicious Anæmia.—GEORGE RIDDOCH, M.D., and JOE PENNYBACKER, F.R.C.S.

J. B., male, aged 52. Postal worker.

January 22, 1935: Fell and struck his right knee. A traumatic synovitis developed and kept him in bed for two weeks, during which time he was first aware of some numbness along the inner sides of both feet. When he returned to work three weeks afterwards, both feet felt numb and he thought his gait was a little unsteady. His fingers too felt tingly, and his hands were a little clumsy in doing up buttons and in writing. From that time, numbness and tingling of lower limbs have spread up to level of lower angle of scapulæ. The legs have become progressively more unsteady and weak. Power of upper limbs not impaired subjectively. No sphincter disturbance. No pain, but during the past six weeks the lower limbs have become very tender to the touch.

General health good: has always been thin, but appetite is fair, and he has only occasional slight flatulent dyspepsia. No history of sore tongue or dysphagia.

On examination.—Thin, wasted-looking man; mucous membranes a little pale. Tongue clean and moist; not atrophic. No enlarged glands palpable. Functions of cranial nerves intact. Fine finger-movements a little clumsy in both upper limbs; no gross weakness, ataxy or dystonia. Lower extremities thin; patient has great difficulty in voluntary relaxation, limbs writhing about restlessly. Gross ataxy in purposive tests; he is unable to walk without assistance. Rombergism present. Considerable generalized weakness of both lower limbs—if anything, more marked distally than proximally. Tendon reflexes diminished in upper limbs, absent in lower limbs. Abdominals present. Plantar responses absent. Anæsthesia and hypo-algesia to cotton-wool below knees. Position sense absent in both lower limbs. Vibration sense lost up to costal margins. Muscles of calves moderately tender to pressure. Number of circinate areas of brown pigmentation in skin of lower abdomen; present two weeks prior to admission.

Blood-count: R.B.C. 3,760,000; Hb. 79%; C.I. 1·05; W.B.C. 5,600; Halo 7·5 mm. Test meal: achlorhydria. Cerebrospinal fluid: Clear; no cells; total protein 0·050%.

Wassermann reaction negative in blood and cerebrospinal fluid.

Peripheral Neuritis, probably due to Diphtheritic Infection of a Wound of the Foot.—GEORGE RIDDOCH, M.D., and JOE PENNYBACKER, F.R.C.S.

F. D., male, aged 17, sheet-metal worker.

Four months ago: Stuck a nail in the sole of his left foot; the wound became septic and developed into a cellulitis of the foot, with inguinal lymphadenitis. Was in bed for two weeks; wound took six weeks to heal.

Three months ago: Feeling of pins and needles in both feet; this rapidly spread up both legs to the knees. Legs got tired easily, feet felt heavy, and knees occasionally gave way with him.

Two months ago: weakness of lower limbs was at its height. Had difficulty in walking without support. Fingers began to feel numb and clumsy; grip rather weak. For two weeks his vision became misty for near objects and he could not see to read properly. His voice grew husky and at times he seemed to be talking through his nose. No difficulty in chewing or swallowing; no nasal regurgitation.

One month ago: Began to improve; improvement was rapid and is now almost complete subjectively. Now complains simply of some tingling in his toes, soreness and tenderness in calves and soles, and a little weakness of both lower limbs.

No history of sore throat or diphtheria-contact.

On examination.—Well-nourished, healthy-looking youth. Nose and throat healthy. Nasal and throat swabs negative for Klebs-Löffler bacillus. Schick reaction negative. Functions of all cranial nerves now normal. Slight weakness of both grips, extensors and flexors of wrists and fingers.

Lower limbs: Slight symmetrical weakness of both anterior tibial groups, not of a degree to produce any functional disability now, except early fatigue. Small muscles of feet tender to pressure. Gait and stance normal. Tendon reflexes all absent. Abdominals present, plantars flexor. Sensation: slight hypo-algesia over terminal phalanges of fingers, and over lower limbs up to level of knees. Posterior-column sensibility intact. Cerebrospinal fluid clear, three cells, total protein 0·150%. Wassermann reaction negative in blood and cerebrospinal fluid.

Hypertrophic Peripheral Neuritis.—GEORGE RIDDOCH, M.D., and JOE PENNYBACKER, F.R.C.S.

W. R., aged 42, male, railway carriage cleaner.

Well until two years ago when he noticed wasting of both hands and, shortly afterwards, weakness of grip. From that time there has been a progressive wasting, and proportional weakness of both upper limbs. From the outset his hands have felt numb and stiff, as if they had been squeezed, but sensibility is still subjectively intact.

One year ago, his feet began to feel numb, and from that time both lower limbs have wasted and become very weak. He has to look where he is putting his feet, and is very unsteady in the dark.

No sphincter disturbance. General health quite good, but he has lost about 2½ st. during the past two years. No family history of any allied affection.

On examination.—Thin face; prominent eyes (? since onset of this disease). Afebrile. Pulse-rate 80 to 90 per minute. Pupils rather small; right smaller than left. Reaction to light is incomplete and poorly sustained; that to accommodation-convergence is fuller and better held. Functions of other cranial nerves intact.

Upper extremities: Symmetrical wasting and flaccidity, with proportional weakness, more marked distally (small muscles of hand) than proximally. Fibrillation of all wasted muscles, which are tender to pressure. Trunk: Thoracic and abdominal muscles contract powerfully and symmetrically. Lower extremities: Symmetrically wasted and flaccid. Wasting affects feet and legs rather more than thighs, and weakness is more marked distally than proximally. Considerable ataxy in gait and purposive tests. Rombergism present. Reflexes: All tendon reflexes absent. Abdominals present. Plantars flexor, right and left. Sensation: Light touch and pin-prick impaired over distal parts of hands and feet. Position and joint sense very defective in both hands, and feet. Vibration sense lost in hands and feet; impaired over proximal bony prominences. Peripheral nerves: Considerable uniform thickening of median, ulnar and radial nerves in upper limbs, and of femoral and peroneal nerves in lower limbs.

Cerebrospinal fluid: Queckenstedt ? positive; three cells. Total protein 1·8%. Fluid yellow. Wassermann reaction negative in blood and cerebrospinal fluid.

Blood-count, skiagram of spine, urine, fæces, alimentary functions: all normal.

Discussion.—Dr. RIDDOCH: I will discuss these three cases together.

The first is a case of polyneuritis associated with Addisonian anæmia. We brought it forward in order to suggest that an obvious change in nomenclature might be made for conditions which ought not to be called subacute combined degeneration of the cord. It is a case mainly of peripheral neuritis, associated with pernicious anæmia and achlorhydria, but it is difficult to give it a distinctive name. To call it "anæmic polyneuritis" would be wrong, and to speak of it as "deficiency polyneuritis" would be equally wrong, because other varieties of polyneuritis are associated with anæmia and "deficiencies."

The chief point of interest in the second case is that while the weakness and numbness in the hands and legs were increasing, the boy developed defective vision, especially for near objects, which lasted two weeks. We raise the question as to whether the attack of misty vision was due to cycloplegia, and, in consequence, whether the wound was infected with diphtheria organisms. The story is suggestive. The Klebs-Löffler bacillus may infect wounds in the extremities. In Egypt, during the late war, such cases were described by Walshe, and in those cases cycloplegia occurred with polyneuritis.

Our last case is one of hypertrophic peripheral neuritis in a man of 42, without, so far as we can ascertain, any family history of a similar disorder. The exophthalmos, which is an unusual feature, was present in Boveri's case, and is difficult to explain, for in our patient there were no obvious signs of hyperthyroidism. The defective reactions of the pupils to light and the nystagmoid movements are recognized to be not uncommon accompaniments of this form of polyneuritis. The cerebrospinal fluid findings are, however, of considerable interest. There was, in the first place, a partial block to Queckenstedt's test, and, secondly, the fluid was yellow and contained a high percentage of protein and few cells.

What is the explanation of the obstruction in the subarachnoid space? Is it due to chronic arachnoiditis associated with the nervous lesions and, in consequence, is the whole condition inflammatory in origin, or is it the result, as Dr. Russell Brain suggested, of enlargement of the posterior roots?

Dr. HUGH G. GARLAND said he had encountered a considerable number of cases of hypertrophic neuritis, especially in orthopædic out-patient departments. Usually the patients were suffering from claw-foot, and the neurological side of the case was usually overlooked. The nerve hypertrophy in Dr. Riddoch's case was remarkable, but he did not agree that there were no signs of thyrotoxicosis, as the man had lost a good deal of weight, and had a rapid pulse. He suggested an investigation of the basal metabolic rate. With regard to the family history, he had found that on inquiry something was wrong in the relatives in a large number of cases. He had often found in brothers and sisters of cases of hypertrophic neuritis that they had no tendon-jerks. With regard to plantar responses, they were often doubtful in patients suffering from claw-foot.

The PRESIDENT, referring to Dr. Riddoch's request for a separate terminology for his first case, said he was not convinced that the lesion was entirely peripheral. It was difficult to distinguish peripheral from central lesions, especially in cases of this flaccid type. The disease knew no distinction between the peripheral nerves and the roots and columns of the cord. Such a case could be called one of "neuro-myelitis."

Retinal Hæmorrhages, of Doubtful Ætiology.—J. H. HUNT, M.D.

M. E., female, aged 18. Admitted to hospital on April 3, 1935, under the care of Dr. Grainger Stewart.

History.—November 29, 1934, she awoke in the morning to find that the vision of her right eye was "blurred and misty" in the lower nasal quadrant of the visual field. This visual defect persisted.

December 19, 1934: Admitted to the National Hospital when examination of visual fields revealed in the right eye a lower nasal quadrantic defect. Retinoscopy: In the right fundus a large area of degenerated retina in the distribution of the superior temporal artery, with patches of exudate and many small hæmorrhages.

From the upper part of the macula there was a well-marked macular fan. General examination revealed nothing abnormal. Blood-count normal.

Vision in the right eye slowly improved until February 22, 1935, when she awoke in the morning to find the vision in her right eye again impaired, and the eye a little "sore."

On examination.—Heart normal. Blood-pressure normal. General examination negative. Visual acuity: Right $\frac{6}{18}$; left $\frac{6}{6}$; visual field of right eye showed a defect larger than on previous admission.

Right fundus: Large pools of blood over superior temporal, superior nasal and inferior temporal areas of the retina. Macular fan as before.

Blood-count, blood-platelet count, coagulation time and bleeding time, all within normal limits. Skiagrams of skull, cranial vaults, and nasal sinuses normal. Cerebrospinal fluid normal. Blood Wassermann reaction negative.

Progress.—The changes in appearance of the hæmorrhages since the patient's admission to hospital can be seen in drawings of the fundus.

Possibly this is a case of Eales's disease. The cerebrospinal fluid is normal, as also are the blood-platelets, and the general examination is negative. The cases which Eales described, in 1886, were mostly in young men, and the hæmorrhages were partly in the vitreous. In this girl they are mostly subhyaloid. If these hæmorrhages cease, what is the prognosis as to recovery of sight in the part of the retina where the hæmorrhages have been occurring? What treatment ought to be given?

Dr. RUSSELL BRAIN said that similar cases were referred to him from time to time at the Royal London Ophthalmic Hospital. They were met with in both sexes. Usually the subjects were young adults. Sometimes the hæmorrhages were retinal, sometimes they were mainly vitreous. The patients always appeared to be normal in other respects. As the hæmorrhages became absorbed a good deal of improvement in vision might occur, but he would not like to hazard a prognosis in this case.

Increased Intracranial Pressure: Case for Diagnosis.—N. S. ALCOCK, M.B.

H. K., male, aged 44. Admitted under the care of Dr. Hinds Howell on 30.4.35. Nothing of note in past or family history.

In November 1934, pain and swelling developed in the left leg; the condition was diagnosed as phlebitis, and the patient was in bed for eight weeks. When he got up the condition recurred, and he also began to have headaches. These were continually present, worse at night, and situated behind his eyes. He also began to be sick, chiefly after meals.

He was admitted to the General Hospital, Nottingham, where he was found to have enlarged pelvic glands above Poupart's ligament. The headache continued.

One week after admission, the right leg swelled up as the left one had done.

25.2.35: He passed 1 to 2 oz. of pus per rectum. Nothing abnormal felt on rectal examination.

W.B.C. 12,800; polys. 77·5%; lymphos. 20%; cerebrospinal fluid albumin 0·09%.

30.3.35: Noted to have bilateral papillœdema, 3D in right eye; 1D in left.

Examination on admission.—Bilateral papillœdema. Nystagmus on lateral deviation both ways. Left angle of mouth not quite so well withdrawn as right. Slight unsteadiness in arms.

Blood-count: R.B.C. 4,120,000: Hb. 70%; C.I. 0·85; W.B.C. 7,400; polys. 74·5%; lymphos. 25·5%.

Cerebrospinal fluid pressure 295 mm., 2 cells; total protein 0·07%; otherwise normal.

Blood-urea 38 mgm.%. Skiagram normal.

Progress.—For the last four or five weeks he has definitely improved; his headache is less, and he feels much better. Signs are unchanged.

A suggestion has been made that this might be a case of poisoning by lead, as for three nights the patient had stomach-ache and colicky pains, and has previously had similar pains. There is no punctate basophilia, and there is nothing in his occupation to suggest lead poisoning.

Discussion.—The PRESIDENT said that papillœdema in lead poisoning was more common in children than in adults. He thought that the condition in this might be a "pseudo-tumour," or rather an arachnitis circumscripta.

Dr. ALCOCK said that since the patient had been in hospital the measurements had not changed.

Paget's Disease with Spinal Compression, improving after Laminectomy.—J. H. HUNT, M.D.

H. W., male, aged 60. Admitted January 23, 1935, under the care of Dr. Grainger Stewart.

History.—Four and a half years ago: Onset of aching pains in both shoulders and both hips. Three and a half years ago: Gradual onset of weakness of both legs with a girdle sensation round the chest. Two years ago: Unable to walk without support. Six months ago: Cramps in abdominal muscles and legs. Hesitancy of micturition.

On examination.—Paget's disease of clavicles, tibiæ, femora and pelvis. Wasting and paralysis of the lower six intercostal muscles. Sensory level, D 5 — with anæsthesia, analgesia and loss of vibration sense below this, and slight "sacral sparing." Abdominal reflexes absent. Frequent and very painful flexor spasms of the legs. Complete spastic paraplegia. Skiagram of spine revealed typical Paget's disease of the upper dorsal vertebræ. Lipiodol introduced into the cisterna magna was held up at the level of the second dorsal vertebra.

March 8, 1935: Laminectomy by Mr. Julian Taylor, D 2, 3, 4 and 5. Laminæ thickened and soft, compressing the theca in the upper part of the wound.

Progress.—Since operation the spasms have markedly diminished both in frequency and severity. The sensory level is lower, with more sacral sparing. A little change in the motor power of the legs has occurred.

I have seen two other cases like this recently; the patients both died soon after the operation. There was some question in this case whether operation was advisable. The patient has improved considerably. The spasms are less, he is more comfortable, and muscle movements are beginning to return. I would like to be informed by anyone who has seen a long series of cases, as to what proportion improves after laminectomy.

Discussion.—Dr. RIDDOCH said that it was important to consider the radiological evidence. He had had several cases of the kind; some had done well, others, badly. An important consideration from the surgical standpoint was that a collapse of the bony covering of the spinal cord might easily occur in the stage when the bone was soft, rather than in the later stage, when it was sclerosed. It might be advisable to put the patient into a jacket when he got up, as in cases of spinal caries.

Mr. HUGH CAIRNS said that one of the big factors in such a case was the duration of the paraplegia. The results in the cases in which he had operated had been, for the most part, gratifying. The operation was a tedious one, the laminæ being so much thickened and so vascular, but once the exposure of the dura was brought about, even narrow exposure, and pulsation began to occur in it, the patient would recover from paraplegia provided the operation had been done early. In one case of Dr. Riddoch's the patient had been paralytic for several years before operation, and in that case no improvement had taken place after laminectomy.

Mr. JULIAN TAYLOR said that he agreed with Dr. Riddoch about the X-ray signs. The disease was progressive, beginning with an actively growing fibrosis of the bone and

finishing in a dense sclerosis. Eventually the bone became brittle. It was not a case of bending of the spinal canal or of the pressure, but was an actual concentric narrowing, owing to increase in size of the bone. As Mr. Cairns had indicated, the prognosis depended on the severity of the paraplegia before operation, but it also depended on the stage that the disease had reached. He had known recurrence of paraplegia follow about eight years after successful operative relief, the recurrence being due to progress of the Paget's disease in the vertebral column.

The PRESIDENT said an important consideration was the progressiveness of the original disease; he would like to know how long cases had been followed.

Dr. RIDDOCH (in reply to the President) said he was not able to say, offhand, how long his patients had remained reasonably well after laminectomy, but he had not had one who had done so longer than the patient in the case mentioned by Mr. Julian Taylor.

Left Temporal Cholesteatoma.—J. MCDONALD HOLMES, M.R.C.P.

C. H., aged 33, male. Admitted under Dr. Kinnier Wilson.

Family history.—Nothing of note.

Past history.—In 1919, at the age of 17, onset of fits, followed by headache, usually at intervals of one or two months. Diurnal fits preceded by a general frightened state for about an hour. Is partly conscious during a fit.

Nocturnal fits. No aura. He knows he has had a fit by the intense headache down the left side of his face, which lasts during the whole of the next day. He has loss of sphincter control and bites his tongue during a fit. During the last few years fits have occurred every twelve or fourteen days. They now begin as a twitching on the right side of the mouth. This spreads from the lips to the tongue and after about two minutes speech is lost. At the same time the patient loses sensation in his right arm. After a fit he feels well again in about five or ten minutes. On one occasion he had diplopia. Occasionally the fits have been preceded by an unpleasant smell. Vomiting sometimes occurs after meals.

On examination.—Marked bulge in left parieto-temporal area, pushing left ear out and down, and giving head a very asymmetrical appearance. Hearing poor in left ear. Marked tremor of outstretched right arm. Sensation normal in all forms. Reflexes normal. Blood-pressure 125/85.

Skiagrams show definite bulging of left temporal region and shadow of what was subsequently found to be a cholesteatoma.

Cerebrospinal fluid clear and colourless; no cells seen; total protein 0·12%. Lange 0001122100. Wassermann reaction negative.

Operation.—A left temporal exploration was performed on April 4, 1935, by Mr. Geoffrey Jefferson. A large cholesteatoma was found, extending along the floor of the middle fossa to the parasellar region. This was evacuated almost completely, but it was found impracticable to remove the cyst-wall owing to its proximity to the internal carotid artery and cavernous sinus.

Six weeks after the operation an aseptic meningitis developed, and the wound had to be opened again. Two ounces of grumous material were evacuated, and the meningitic signs rapidly subsided. Since the operations the fits have diminished in frequency and severity, and since the second operation there have been no fits, apart from slight facial twitching.

Discussion.—Dr. MACDONALD CRITCHLEY said he was under the impression that the term "cholesteatoma" had now passed into oblivion, surviving perhaps only amongst otologists. It was a word entirely without pathological precision when applied to cerebral tumours. More than one type of cerebral tumour contained cholesterin. The cholesteatoma of aural surgeons was different from the cholesteatoma of the veterinary surgeons, and different again from the tumour under consideration. The Americans followed Cruveilhier in calling them "pearly tumours." Perhaps the most satisfactory term was "epidermoid," as affording a clue to the histogenesis, the association with dermoid tumours being a close one.

Dr. RIDDOCH, referring to long histories, said he remembered his first case of cholesteatoma, upon which Mr. Trotter had operated ten years ago. The patient, a woman aged about 60, gave a history of at least 15 years' duration of the condition. She had a stormy post-operative course, but ultimately recovered. The tumour had filled up the posterior fossa, causing multiple cranial nerve palsies.

Osteitis Fibrosa of Right Frontal and Sphenoid Bones.—JULIAN TAYLOR, F.R.C.S.

Joan B., a schoolgirl, aged 12.

History.—Three years ago, whilst at play, collided with another girl whose chin, it is said, hit the patient's forehead. She continued to play and felt none the worse for this trivial accident. During the subsequent months a swelling arose at the site of this impact. The swelling has slowly increased in size and the patient now complains of intermittent stabbing pain in the swelling. This pain is very infrequent and was last present at Christmas 1934. She states that for the past twelve months the vision in the right eye has been failing and that she has to tilt her head to the left in order to view objects clearly out of the right eye. This defect has hardly progressed during the last year. There has never been any weakness, giddiness, nausea or vomiting. She has always worn glasses.

Present state.—Normally developed girl ; average intelligence ; afebrile ; temperature and pulse normal. There is a hemispherical swelling over the right frontal eminence, about an inch and a half in diameter. Its superior limit rises rather abruptly from the skull, whilst below and laterally it merges gradually into the surrounding bone. The swelling is bony in consistence, and is painless. The anterior portion of the superior temporal crest is broadened and more prominent on the right than on the left side. The right temporal fossa looks slightly fuller than the left. The overlying skin is freely movable and of normal appearance, except for a few dilated veins not present on the other side. The central nervous system is normal and there are no other physical signs.

Ophthalmological report (Mr. Humphrey Neame).—Right : Vision, finger-counting at one foot. No definite perception of 2·5 cm. red or yellow discs at one foot ; even three-inch coloured cards give very uncertain results. Field-to-hand movements good. Disc pale (primary optic atrophy) with a myopic crescent on the temporal side. Left disc healthy. The perimeter charts do not show any gross deviation from the normal.

Cerebrospinal fluid not under pressure, no abnormal constituents, Wassermann reaction negative.

X-ray examination.—There is a dense bone-like opacity filling the region of the sphenoidal sinus and projecting upwards behind the roof of the right orbit. There is also a rounded projection from the right temporal region and mottled appearance of bone in this region. Skiagrams of remainder of skeleton show no abnormality.

25.4.35 : Ventriculography revealed no abnormality in ventricular system.

Diagnosis.—Before ventriculography I thought the case to be one of diffuse invasion of the skull from a dural endothelioma underlying the boss on the forehead. Ventriculography, however, having demonstrated that there was no deformity of the ventricles, I now regard the case as one of osteitis fibrosa of the skull.

Proposed operation.—I propose at a first stage to remove a right frontal bone flap, to kill it by boiling, in order to arrest the process of disease in the bone, and at a second stage to attempt to remove the tumour growing in the anterior fossa.

POSTSCRIPT. *Subsequent history.*—The proposed operation was carried out, the right frontal boss being exposed, and cut off the underlying bone with a chisel. A right frontal bone flap was then cut, removed, and boiled in water. The whole disease appeared to be on the external surface, the internal surface having a normal appearance. The boiled bone was replaced and the wound closed. A week later

the wound was reopened, when it was noted that the bone, which after boiling had had a grey colour, was now of the cream colour of the normal skull, and that after the lapse of a short time, small points of blood could be seen oozing from it, showing that it was now vascularized. The bone was again removed, some difficulty being experienced in detaching it from the underlying dura to which it was tightly adherent by granulation tissue which bled profusely. The dura was then raised from the anterior fossa when a smooth rounded mass of bone, about 2½ cm. in diameter, was seen. The cribriform plate could be identified, but none other of the normal bony features of the region. The swelling was excavated with an electrically-driven burr and was removed by cutting away the shell left with a hammer and chisel. After removal of the bony mass, about a centimetre of the optic nerve could be seen lying in its canal. On the following day the child had no vision in the right eye, but subsequently sight returned and it is now (August 1935) said to be slightly better than it was before operation.

Microscopic examination.—Portions of both the bony swellings were examined and they showed similar appearances. That from the forehead consisted of trabeculæ of bone lying in a mass of cellular fibrous tissue. The intracranial mass had similar appearances but in conformity with its greater density, there was more bone and less fibrous tissue. Both were considered to be characteristic of osteitis fibrosa.

? Primary Oligodendroglioma of Brain with Spinal Metastasis.—JOE PENNYBACKER, F.R.C.S. and S. BEHRMAN, M.R.C.P.

E. S., male, aged 21. Admitted, 5.5.34, under the care of Dr. C. P. Symonds, complaining of attacks of severe frontal headache for three months; vomiting, one month; attacks of transient blindness, two weeks; diplopia, one week.

Condition on examination.—Bilateral papillœdema, 5D right and left. Visual acuity $\frac{6}{9}$ right and left. Weakness of both external recti; conjugate upward movements very defective. No nystagmus. Pupils large; slightly irregular in outline; react very poorly to light, better to accommodation-convergence. Cranial nerves otherwise normal.

Limbs: hypotonic and tremulous, no ataxy or lateralized weakness. Tendon reflexes present and equal. Flexor plantar responses.

11.5.34: Subtentorial exploration by Mr. Julian Taylor. Cisterna magna distended, no herniation of tonsils. Cerebellum appeared normal. Operation relieved headache and vomiting, and papillœdema subsided, but there was no change in state of ocular movements.

1.7.34: Readmitted because of persistent vomiting. Decompression tense, not bulging. Physical signs as before. Course of deep X-ray therapy was begun and vomiting ceased almost immediately. Later there was a definite improvement in the reaction of pupils to light and the pupils became more nearly of normal size. Increased range of upward conjugate movement of eyes.

24.8.34: Discharged; free from symptoms and feeling perfectly well. Resumed his work six weeks later and remained in good health until

1.2.35, when he began to suffer from a severe aching pain low down in the back and at times shooting through the buttocks and down the back of the thighs.

1.4.35: Readmitted in very severe pain. Lumbar spine almost immobile and very tender to pressure. No weakness of lower limbs. Hypalgesia on both sides of body below 10th dorsal segment. Left knee-jerk and right ankle-jerk diminished; other tendon reflexes present and equal. Flexor plantar responses. Incomplete spinal block.

Laminectomy 9.4.35 (Mr. Harvey Jackson).—At level of 10th to 12th dorsal laminæ a soft fleshy neoplasm was found, surrounding the cord and infiltrating the

roots of the cauda equina. The tumour, a piece of which was removed for microscopical examination, was reported by Dr. J. G. Greenfield to be a rapidly growing oligodendroglioma.

Mr. HUGH CAIRNS said he thought that the behaviour of the growth was more like that of medullo-blastoma. It was surprising that a patient with oligodendroglioma should have responded so quickly to X-ray therapy without removal of the primary tumour.

Electrical Injury of the Shoulder.—N. S. ALCOCK, M.B.

W. J. C., male, aged 48, admitted to hospital under the care of Dr. C. M. Hinds Howell.

November 23, 1934: While plugging in a face vibro-machine with the left hand, holding an apparatus in the right, he sustained an electrical shock (260 v. D.C.). He felt a tearing pain all over the body, especially in the right arm and shoulder; he was rooted to the ground and unable to release the apparatus. Felt dazed but not unconscious; did not fall. Contact was maintained for about two minutes. No electrical "burns." Immediately afterwards he felt pain, weakness and stiffness in the region of the right shoulder. The pain persisted, and a bruise appeared over the whole of the right upper arm, lasting about ten days, during which the arm was too painful to be moved, and at the end of that time he found he was unable to move the shoulder-joint. He made no progress under physical treatment. A skiagram is said to have revealed splintered bone.

Condition on admission (January 1, 1935).—Marked limitation of movement at the right shoulder-joint, associated with pain; the muscles around the shoulder-joint were wasted. No fibrillation. No sensory loss.

Skiagrams revealed a fissured fracture running through the head of the right humerus. No displacement of fragments. No dislocation of shoulder-joint.

The shoulder has improved under repeated manipulations. The pain has diminished.

Nasopharyngeal Endothelioma.—JOE PENNYBACKER, M.B., F.R.C.S., and N. S. ALCOCK, M.B.

G. B., aged 30, female, admitted 25.4.35, under the care of Dr. George Riddoch.

Twelve months ago she began to complain of deafness of the right ear and medium-pitched tinnitus referred to that ear, slowly progressive. Six months ago she had convergent squint of right eye, with corresponding diplopia. At about the same time she began to have attacks of headache at the back and vertex of the head, recently associated with vomiting. Four months ago a small lump appeared in the right side of neck. Three months ago she noticed that her voice was becoming weak and attempts to swallow solids induced retching. The right side of neck was a little thin. Two months ago: gland removed from right side of neck; said to be "fibrotic, as from an old healed acute inflammation. No evidence of malignancy or tubercle," although the clinical diagnosis had been tuberculosis.

Just after operation, patient noticed a patch of numbness behind right ear; this has slowly spread all over the right side of the face. She has lost about 2 st. in weight in past year.

Condition on examination.—A large, firm, rounded swelling over upper third of right sternomastoid. Another large firm swelling in right oropharynx, displacing soft palate forward and downward. Complete sensory and motor paralysis of right trigeminal nerve. Paralysis of right external rectus muscle. Very little, if any, facial weakness. Middle-ear deafness, right. Paralysis of right side of soft palate and right vocal cord; right side of posterior third of tongue and pharyngeal wall are insensitive. Marked wasting and weakness of right sternomastoid and trapezius.

Tongue not affected. Sensory and motor functions of limbs all normal. No change in reflexes.

Blood-count: R.B.C. 3,880,000: Hb. 76%; W.B.C. 17,200 (polys. 85%, lymphos. 15%). Cerebrospinal fluid: pressure 95; one cell per c.mm.; total protein 0·050%. Wassermann reaction negative in blood and cerebrospinal fluid.

Discussion.—Dr. ALCOCK said that Dr. Pennybacker had shown a similar case in April 1934.[1] In that case X-ray therapy had been tried without success, but it might be suitable in the present case.

Dr. G. RIDDOCH said there was some question as to whether deep X-ray therapy would be advisable.

[1] *Proceedings*, 1934, xxvii, 1351 (Sect. Neurol., 47).

Section of Dermatology

President—HENRY MACCORMAC, C.B.E., M.D.

[*May* 16, 1935]

Mycosis Fungoides.—G. B. DOWLING, M.D., and W. FREUDENTHAL, M.D.

Male, aged 40. Three years ago the lower jaw was fractured in an accident. Eight months ago a swelling developed at the site of the fracture, broke down, discharged for a while, and eventually healed. Two-and-a-half months ago a swelling appeared on the right arm, and another on the right anterior axillary fold; a third appeared six weeks ago, on the front of the right leg, below the knee. During the past few days the swelling over the lower jaw has recurred.

The lesions, at first, were firm circumscribed tumours, hardly different in colour from the normal skin, but by degrees developing a rather deep red colour. They cause the patient no pain or irritation, and that on the right leg had attained the size of a small hazel nut before he noticed it. The clinical appearance suggested the diagnosis of a tumour, possibly mycosis fungoides d'emblée or sarcoma. Two biopsies have been made from the same lesion, the second a month after the first.

First biopsy: The whole cutis is greatly changed by a cellular deposit. These cells are arranged in densely packed nests, of various shapes and sizes, occasionally following the course of vessels, connected by a network of cells invading the spaces between the bundles of collagen tissue. By higher power the individual cells are seen to be oval or spindle-shaped, except where they are faceted by pressure. They have a deeply-stained nucleus and a small area of protoplasm. Although the elastic fibres are diminished they are not destroyed to such an extent as might be expected in a simple inflammatory condition. The changes in the epidermis are slight and apparently secondary.

Second biopsy: The cellular infiltration is even more dense than in the first, and the cells are more varied in size and shape. In some places a formation suggesting granulomatous tissue is to be found. I suggest a mesoblastic growth, as, e.g. in Hodgkin's disease, or in mycosis fungoides, the latter being the more probable.

Discussion.—Dr. J. M. H. MACLEOD said that judging from its microscopical appearances he did not think the growth was sarcoma. The cells were a little irregular in size and shape; the nuclei were not very well shown in the stainings. He thought the appearance was more like that of mycosis fungoides.

Dr. DOWLING (in reply) said that Dr. MacLeod's opinion confirmed the diagnosis at which Dr. Freudenthal and himself had already arrived, especially on the microscopical evidence.

Morphœa.—G. B. DOWLING, M.D., and W. FREUDENTHAL, M.D.

The patient, a man, aged 75, first noticed marked irritation and a few white spots, about nine months ago. The lesions have gradually increased and now number about twenty, occupying a zone corresponding to the ninth and tenth thoracic segments. They are small, irregular in shape, white, superficially sclerosed and, in some cases, surrounded by a faint pink or bluish pink border.

The diagnosis of sclerodermia of segmental distribution or atrophic lichen planus was made.

Microscopical report (W. F.).—In the upper third of the cutis the collagen tissue is thickened, the bundles are caked together, sclerosed. A moderate inflammatory reaction is seen below this area. The horny layer is considerably increased and shows horny plugs; some of these fill up funnels.

The histological appearance is identical with that seen in circumscribed sclerodermia. In similar cases discussion has arisen over the diagnosis, as to whether the condition was sclerodermia or lichen planus atrophicus. In the investigation of these border-line cases, histological examination would perhaps help to elucidate the diagnosis. Following the discussion on the case shown by Dr. Wigley in December last,[1] I have been interested in the question and propose to study it. I should be pleased to receive sections from such cases, either recent or old.

Discussion.—Dr. F. PARKES WEBER remarked that the first thing noticed by the patient himself was a troublesome local itching, and that still persisted. He had never seen morphœa in a man 75 years of age; nor was he aware of such a case having been reported. He regarded this as a case of "névrodermite" in an old man who was always scratching the itching region.

Dr. DOWLING (in reply) said that in neurodermatitis one would expect to find lichenification. In this case there were discrete, superficially sclerosed spots and not a trace of lichenification. The diagnosis had been made by Dr. Freudenthal on the histology alone.

Tumour (? Fibrosarcoma) of Abdominal Wall: Case for Diagnosis.—C. H. WHITTLE, M.D.

G. R., a married woman, aged 63.

History.—Probably about thirty years ago a cyst was removed from the abdominal wall just below the sternum. Since then the scar has been gradually increasing in size, and when first seen by me in May 1934, it had been tender for a few months. At that time there was an area of skin about 4 in. by 3 in. replaced by raised tough tissue of keloidal type. The patient was under the care of Mr. Bowen, who removed a small portion at the lower part for biopsy, the report of which is given below.

After treatment by radium the swelling became flatter for a short time, but three months afterwards it began to grow larger and there was a cystic area in the upper part of the tumour. The swelling and infiltration are in the skin and subcutaneous tissue and the tumour has recently appeared to be more active at the upper edge.

Report on biopsy (June 1, 1934).—This tumour in section shows many interlacing bundles of actively growing young fibroblasts, with some rather primitive blood-vessels, but the older parts show the more characteristic hyaline fibrous bands and well-formed vessels usually found in keloid. I think this is a rather neoplastic type of keloid.

Treatment.—Acting on my report, in June 1934, the surgeon applied radium—12 needles of 1 mgm. each embedded in the tumour for five days (=1,440 mgm. hours). The result of treatment has not been very satisfactory as the tumour is undoubtedly increasing in size.

Discussion.—Dr. FREUDENTHAL suggested the diagnosis of fibrosarcoma.

Dr. ROBERT KLABER agreed with Dr. Freudenthal. The growth might well be fibrosarcoma (which was perhaps better described as a recurrent fibroma, or Schwannoma) as such tumours were believed to arise from this nerve sheath.

If the condition had been a keloid, one would have expected to see a keloidal change in the biopsy scar. He had not, however, previously seen cystic changes in these growths.

Dr. A. M. H. GRAY said he did not think this was keloid: the thickening, he considered, was not in the skin, but rather in the subcutaneous tissue. The skin could be definitely moved over the swelling in the upper left part of the tumour. There was a good deal of atrophy, which was probably due to radium.

Dr. WHITTLE (in reply) said there was no information available as to the nature of the previous tumour. The biopsy examination was made in June 1934. Since then the tumour had grown larger. On that account, and in view of what had been said, he withdrew the term "keloid." He also inclined to the idea that the growth was probably fibrosarcoma.

1 *Proceedings*, 1935, xxviii, 506 (Sect. Derm., 24).

Arsenic-resistant Syphilis.—H. MACCORMAC, C.B.E., M.D. (President).

These two patients, a man and a woman, illustrate in an unusually complete way the theory of the existence of a special type of *Spirochæta pallida* which is relatively resistant to the arsenical drugs, and whose resistant qualities are retained when the spirochæte is transmitted from one individual to another.

The woman is aged 28 and is single. She states that she first noticed an eruption on the palms in December 1934. I saw her at Middlesex Hospital in January 1935. She had then an extensive polymorphous eruption, a florid secondary syphilide, with a strongly positive Wassermann reaction. Treatment with novarsenobillon was at once begun. She received seven intravenous injections (total 3·9 grm.); developed vomiting and pains in the legs, upon which the arsenic was discontinued. Since then she has received ten injections of bismuth. In spite of this intensive treatment, extending over seventeen weeks, the eruption on the arms and face became more pronounced and more extensive than it was originally, indeed it has behaved exactly as if the patient had been untreated.

The second patient, a man aged 26, cohabited with the first patient and contracted syphilis from her. He observed a genital sore in December. When he attended the hospital in January, his condition was clinically primary syphilis, although both the spirochæte and the Wassermann tests were negative. Treatment was begun at once with ten intravenous injections of novarsenobillon. After the eighth injection a characteristic secondary syphilide appeared on the forehead. The Wassermann reaction was strongly positive at the end of February.

Members of this Section are aware of the work of Drake and Thompson, who were the first in this country to direct attention to the arsenic-resistant group of spirochætes, and their observations agree with those of many continental dermatologists. The two cases I have brought to-day have a special, and I believe unusual, bearing upon this problem, because they are partner cases showing, first, the reaction of the arsenic-resistant spirochæte, and secondly, that the acquired quality is transmissible—i.e. the type breeds true.

I remember during the War discussing, in France, a problem of syphilis with the late Sir John Rose Bradford: he mentioned the curious fact that shrimps were liable to a venereal disease, and that when thus infected they became luminous. If we had some similar way of distinguishing people with this resistant spirochæte it would be an advantage, for in this form it presents a new problem with which we are unable at present to cope, except, as I believe, in the use of mercury, preferably by inunction.

Discussion.—Dr. A. C. ROXBURGH said that in 1930 he had seen a patient who had acquired syphilis in 1908. Several friends of this patient, infected by the same woman, had already died of the disease. The cases now shown seemed to constitute another instance of a particularly vicious type of spirochæte.

Dr. JOHN FRANKLIN asked whether the President implied that these patients were resistant to arsenic only, or to all forms of treatment. The woman had also had bismuth, which alone, in time, would clear up the cutaneous manifestations of syphilis, therefore he presumed that she was also bismuth-resistant.

Dr. G. PETIT said that he had had a patient with primary and secondary syphilis who relapsed after the first five injections of salvarsan in three weeks; he then had had another course and had relapsed again in three weeks. He had relapsed again after the third course. Numbers of spirochætes were always found. One day the patient was stripped, and it was noticed that the body was somewhat hairless. He showed no other signs of thyroid deficiency but his metabolic rate was 35% subnormal. He was given 1 gr. of thyroid extract daily, and was once more treated for the syphilis, and had no further relapse.

The PRESIDENT (in reply) said that these cases seemed to be resistant to bismuth as well as to arsenic, but not to mercury. The diagnosis could not be questioned; they conformed both serologically and clinically in every respect to early syphilis.

Epithelioma Adenoides Cysticum.—W. N. GOLDSMITH, M.D., and W. FREUDENTHAL, M.D.

R. A., a boy, aged 7½.

Present condition.—On the face, especially round the eyes, and also scattered over the neck, are numerous tiny papules, most of them rather translucent and some with a central dimple. It is particularly interesting that some show an irregular speckling of pigment, whilst others are deeply pigmented throughout. Clinically, therefore, the little papules resemble, in some cases, juvenile warts, in others, molluscum contagiosum, and in others, pigmented moles. The distribution around the eyes suggested the possible diagnosis of Brooke's epithelioma adenoides cysticum.

The following are unusual points in this case: (1) The onset was at the age of 5 years, whereas the usual onset is about puberty or later. (2) Only a small minority of published cases have been in males. (3) In the account of the disease

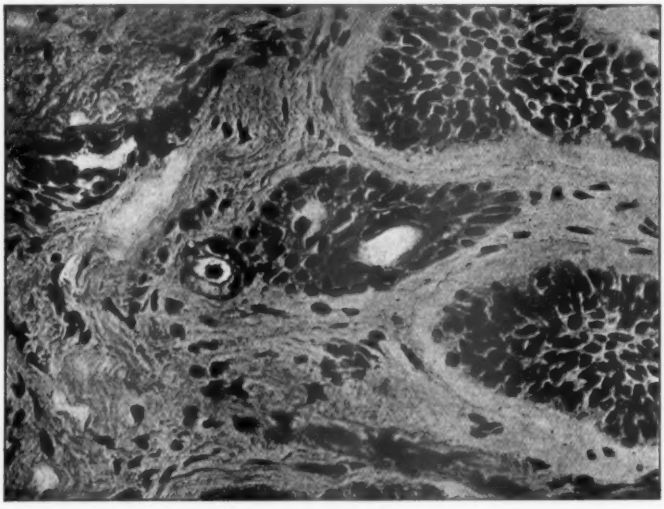


FIG. 1.—In the centre of the picture is a solid neoplastic mass containing an empty hair-follicle and a few sebaceous gland cells. (The hair shaft has been forced away in cutting, but can be seen in the next of the serial sections.)

in Jadassohn's "Handbuch" there is no mention either of central umbilication or of pigmentation.

The umbilicated lesions closely resemble those in a case recently shown by Dr. Corsi at a meeting of the St. John's Hospital Dermatological Society, the histological structure of which was that of pure sebaceous adenoma.

Three clinically different tumours were excised for microscopic examination: (1) An unpigmented one from the forehead, (2) a deeply pigmented one from the eyelid, and (3) one showing moderate pigmentation, from the front of the neck. All three reveal a close histological resemblance and allow with certainty the diagnosis "epithelioma adenoides cysticum."

The tumour consists of two elements: (1) Long narrow processes and branching masses of epithelioma, the cells of which are of basal type, and (2) cysts, many of which contain horny lamellæ in loose concentric layers. In addition many of the cysts contain lanugo hairs, and even in the solid neoplastic masses there are, here

and there, hairs and a few sebaceous gland-cells (fig. 1). Thus, in our case, the connexion with the pilo-sebaceous system is very probable.

The part of the section outside the tumour, which clinically appeared normal, shows an interesting alteration in a hair-follicle. The root of the hair is deviated; it is bent at a right angle to the shaft. High up on the one side of the follicle there arises from its wall an atypical epithelial proliferation of exactly the same kind as that in the tumour. On the other side the epithelial proliferation springs just from the angle formed by the epidermis and the hair-follicle. This finding should be kept in

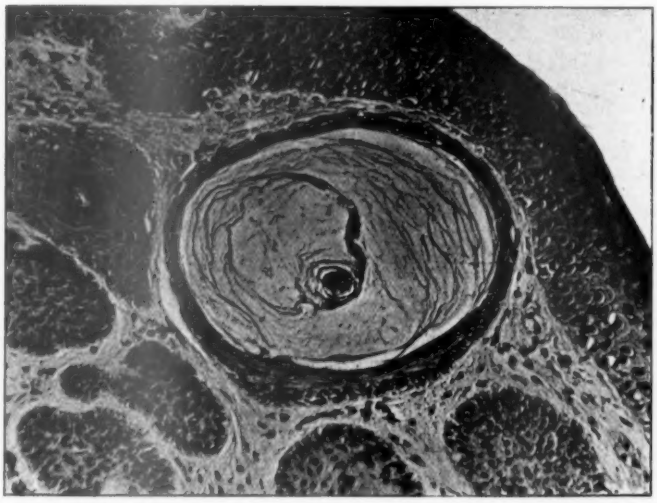


FIG. 2.—Section from the tumour on the neck.

mind whenever there is a dispute as to whether a tumour originates from the epidermis or from its appendages.

In a section from the pigmented tumour on the eyelid, large masses of pigment can be seen both in the connective tissue around the tumour and in the tumour itself; in one place it is so arranged that it might be termed a pigment-pearl.

In a section from the tumour on the neck there is a cyst containing concentric horny lamellæ, and in the centre between the lamellæ is pigment. The pigment probably arises from the melanoblasts of the hair-matrix. The pigment-stream, which normally flows into the hair itself, here flows, in the absence of the hair, between the concentric horny layers (fig. 2).

Discussion.—Dr. I. MUENDE said that in the description there was no mention of the significance of the hyperkeratosis in the centre of the lesion which he (the speaker) regarded as a giant comedo in a dilated hair-follicle. He had had such a case—not yet reported—in which the lesions were similar to those under discussion, though more acneiform. The histology showed a large dilated hair-follicle in which there was a comedo, and from the wall of the follicle one could see epidermal budding resembling that of Brooke's disease.

Dr. KLABER said that there had always been some doubt as to whether or not these small tumours really arose from the pilo-sebaceous apparatus. The microscopic sections in Dr. Goldsmith's case answered this question in a very convincing manner.

Small nodules, the histology of which was closely related, were fairly common on the eyelids of women—the so-called "tricho-epithelioma." Louis Savatard had attempted to

separate this condition, which did not proceed to actual tumour formation, from true epithelioma adenoides cysticum, which usually did so proceed, and in which there was often hereditary influence. This case raised the question as to whether males were also liable to this non-hereditary type, which did not tend to form large tumours.

Dr. GOLDSMITH (in reply) agreed with Dr. Muende that a few of the lesions had a central black speck which might be a comedo-like plug, but no evidence of this had been found histologically. Moreover, in other lesions the dark spots were eccentric and proved to be due to pigment.

Lymphangiectasia of Scrotum.—J. H. T. DAVIES, M.B.

Mr. J. S. B., aged 32. This patient first consulted me on March 27 because of a persistent discharge of milky fluid from the scrotum. He was wearing a suspensory bandage made of jaconet filled with wool, to absorb the discharge. The scrotum was macerated and its whole surface dripped a milky fluid; I filled a test tube in about ten seconds by merely holding the open end against the surface. The composition of this milky fluid according to Dr. L. R. Janes is as follows:—

	%		%
"Reducing substances ...	267 mgm.	Calcium	11·4 mgm.
Urea	37 mgm.	Total solids	7·2 grm.
Non-protein nitrogen ...	83 mgm.	Total fats	0·45 grm.
Total protein...	3·53 grm.	Chlorides (as Cl.)	232 grm.
Cholesterol	Absent		

A white opalescent fluid containing a few red blood-cells and leucocytes. It was not cleared completely by repeated ether extractions and must therefore be regarded as chyloid rather than chylous."

I saw the patient again on May 8 and removed a piece for microscopical examination. Nearly the whole of the surface of the scrotum was evenly studded with cysts, 2 to 3 mm. in diameter, containing an opaque milky fluid. The cysts were lobulated, and in a very large number of them could be discerned hæmorrhagic points. A noteworthy feature was the marked regularity in the size of the cysts and of their distribution over the surface. Dr. Nicholson reports as follows on the section:—

"This specimen shows diffuse lymphangiectasis in the superficial part of the cutis with atrophy of cutaneous appendages, hyaline fibrosis, inflammatory exudate and hyperplasia of epidermis. Slight pigmentation of phagocytes, possibly medicinal."

The patient states that he first noticed a little persistent moisture at the back of the scrotum ten years ago, following a bicycle tour. After a few weeks this dried up but it has subsequently recurred on numerous occasions. Gradually the area involved by these cysts has become larger and the patient thinks that it is still extending. Each successive attack seems worse than the last. A copious discharge may persist for several weeks and then may almost dry up, but the scrotum is never completely dry. When there has been no discharge for some time the fluid in the cysts becomes clear, but while discharge is going on it is always milky. The patient does not think it becomes milky during the digestion of a meal.

My impression is that these thin-walled cysts may be prevented from rupturing by very careful protection of the scrotum, for it is probable that they never rupture spontaneously but only after a slight trauma. It is difficult, moreover, to see what can be done for this patient, as he is anxious to avoid any operative procedure.

Discussion.—Dr. MACLEOD suggested treatment with carbon dioxide snow; he had tried freezing in lymphangioma circumscriptum and definite improvement had resulted.

Dr. A. C. ROXBURGH said that he had a patient with lymphangioma of the forehead, which had been treated abroad, but ineffectively, with carbon-dioxide snow. He (the speaker) had been able to cure it with zinc ionization, but this present patient might regard that treatment as an operation.

Dr. KLABER said that there had been a small series of cases of lymphangioma circumscriptum at St. Bartholomew's Hospital in the previous year. They had shown a satisfactory response to the insertion of radon seeds.

He did not suggest that this would be a very suitable form of treatment in the present case. He did think, however, that this condition also was likely to be radio-sensitive, and that, therefore, X-ray treatment might be employed.

Lupus Erythematosus.—J. E. M. WIGLEY, M.B.

The patient is a healthy girl, aged 16, who gave a history extending over eight years. Her finger- and great toe-nails had gradually broken away, crumbled and disappeared. The process had been practically painless, though she suffers severely from chilblains, and has usually cold hands and feet. The ends of all the fingers of both hands and of both great toes are tapered and dead-white, as far as the posterior nail-folds, beyond which is a narrow erythematous ring extending around the finger. The skin over the tapered end is not hard or, apparently, thickened to the touch. Practically all the nails are completely missing, though a few friable remains are present. These do not present any special characteristics. Along the palmar surface of the right index finger, and on the left heel, is a scaling, bluish area, with some evidence of plugged dilated follicles, very suggestive of the "fixed" type of lupus erythematosus.

Discussion.—Dr. DOWLING said he agreed with Dr. Wigley's diagnosis. He wondered whether this type of case was to be identified with Hutchinson's "chilblain lupus," which he (the speaker) thought came into the category of lupus erythematosus and was found in people with a "chilblainy" circulation. He thought that there was some confusion as to what was meant by that term.

Dr. A. M. H. GRAY said that he also agreed that this case was one of lupus erythematosus, and he thought there was no question that it was similar to the Hutchinson type. The typical variety of Hutchinson's chilblain lupus occurred in the middle of the face and the skin over the nose and cheeks was thin and drawn.

Porokeratosis (Mibelli).—M. J. FENTON, M.B.

Mrs. J. R., aged 33, married, two children. Present occupation: household duties, formerly parlourmaid and cook.

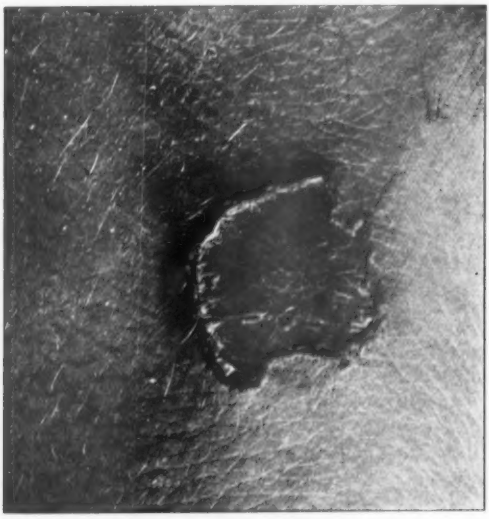
Was born in Ireland, and came to England nineteen years ago. She is a perfectly healthy patient.

History.—She has had a lesion on the back of the right hand, for at least sixteen years. She does not remember much about it, except that it began as a pimple, which she used to scratch. It spread and has remained in its present state for about ten years. It irritates very much, and is always worse after washing in warm soda or soapy water, after which it appears red and inflamed, but it is never affected by cold water. Scratching relieves the irritation. If she keeps her hands out of water for a few weeks, as, e.g. when she is away at the seaside, it appears less prominent and much paler, otherwise there is no difference in its appearance at any particular time of the year, or with any change of temperature.

Description.—A roughly quadrangular lesion on dorsum of right hand, about an inch square, with atrophic, depressed hairless central area. The border is raised, and irregular in outline and depth. Viewed laterally there are waves of warty-like elevations which vary in size—like tiny volcanoes. This border or ridge is very hard, the sweat ducts being filled with a hard material. There is hyperkeratosis near the glandular openings. Close examination of this ridge reveals a groove. It is this "trench" which clinically diagnoses the condition. The central area is depressed, smooth, pink in colour, covered with scattered fine scales, and has the natural epidermal furrows, with no sensory changes. There are no buccal lesions.

An interesting observation is that the patient has neither conjunctival nor palatal reflexes. She has anæsthesia to pin-prick, glib knee-jerks, and the emotional facies. All these features make one think of a neuropathic condition associated with hysteria.

Family history.—Mother died at the age of 36, from tuberculosis, having had 15 children—one set of triplets and one of twins. Twelve have died, one at the age of 19 from tuberculosis, the others either in infancy or early childhood. The patient's sister and brother are both alive, although the latter is not strong. Her parents were not related. There is no family history of skin trouble.



Porokeratosis (Mibelli).
(Dr. M. J. Fenton's case.) Actual size.

The patient first consulted me on account of a keloid on the chest, secondary to a scratch, now of six years' duration.

Treatment.—An excision is the only known satisfactory method of obliterating the condition ; is it advisable in this case, in view of the history of keloid formation after a scratch ?

Microscopic examination will be carried out, and the current literature reviewed at a later date.

Infra-red photography did not reveal any unusual features.

List of Cases recorded in the Dermatological Literature of this Country

Galloway [1], later by Thomson [1A]. Bilateral symmetrical lesions on hands.

Perry [2] showed a case of hyperkeratosis excentrica in 1901. No notes available.

MacCormac and Pellier [3] described a case in 1918, in an English soldier, seen in France, whose condition was thought by the patient to follow on a vitriol burn, a few years previous ; multiple lesions affected left arm, neck, shoulder, hands and fingers, including nails, also the tongue. The presence of lesions on the tongue tend to disprove the sweat-duct theory of the origin of the disease.

Pernet's case [4] shown in 1925 was on the leg—male patient—and from its

description was resembling that described by Wende in 1898—I think it was similar to mine—it also appeared to get better at the seaside.

Of the four cases shown in England, two were males, and one a female. Perry's case not described, and sex is unknown.

There has been no family history occurrence in any of these cases.

As this is the fifth case recorded in English Dermatological Literature, I thought it worth while to show it to the Section.

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1A THOMSON, M. S., *ibid.*, 1932, xliv, 544.
2 PERRY, E. C., *ibid.*, 1902, xiv, 22.
3 MACCORMAC, H., and PELLIER, C. DE C., *ibid.*, 1918, xxx, 197.
4 PERNET, *ibid.*, 1925, xxxvii, 190.

? Parapsoriasis-en-Plaques of Brocq.—R. T. BRAIN, M.D.

T. V., a married woman, aged 50, states that her skin has been irritable for about fifteen years. In September 1933 red spots appeared and she has not been entirely free from them since. They are blotchy in appearance and become prominent after a hot bath; they are much less conspicuous when the skin is cool. The irritation varies greatly and appears to be definitely related to the patient's interests and activities. The pruritis may be described as severe.

Her previous health has been invariably good, although she has had frequent headaches which have seemed less troublesome since the skin eruption appeared. She has had three children; a girl, aged 18, and a boy, aged 14, are well; the other child died at the age of 5 months from cardiac malformation. Her menstrual periods are normal and still regular.

It was thought that the eruption was a premycotic one, and six doses of X-rays were given on August 1, September 18, and December 5, 1934, and on February 14, March 18, and April 15, 1935. Doses of 2 p.d., measured above 2 mm. of aluminium and doses of one-third pastille without a filter, were given to areas on the thighs, neck, shoulders, axillæ, and waist. Irritation was more relieved by X-rays than by other applications, and for a time the red patches were less obvious. Marked pigmentation followed the irradiation and has persisted.

The patient's local doctor treated her with bromide, novarsenobillon 0·3, 0·45 and 3 × 0·6 grm., and emollients.

On December 12, 1934, she was seen at St. John's Hospital, and the skin condition was very similar to the present. Dr. Muende reported that the Wassermann reaction was negative and that the histological evidence from a biopsy was not definite.

Blood-count (April 25, 1935): R.B.C. 4,640,000; Hb. 90%; C.I. 0·9; W.B.C. 8,600. *Differential*: Polys. 64%; small lymphos. 19%; large lymphos. 12%; monos. 2%; basos. 1%; eosinos. 2%.

At the present time the patient's general condition is apparently good, although she becomes fatigued easily. The skin lesions are most numerous on the trunk and the near parts of the limbs. The face is clear and always has been so. The predominant lesion is an irregular, slightly raised plaque of a dull red colour, varying greatly with the skin temperature. Some of the lesions are slightly lichenized and others definitely eczematous, and at times they seemed to be almost urticarial. Moderate pityriasis capitis is present, and a few lesions on the neck have scales like seborrhoids, but although there is a flexural distribution no other resemblances can be found.

Discussion.—Dr. A. C. ROXBURGH asked whether other members had seen parapsoriasis-en-plaques with the rather raised urticarial appearance of the lesions in this case. He had always thought that the lesions in that disease were perfectly flat.

Dr. MACLEOD said that the lesions of parapsoriasis-en-plaques were not raised. It was very difficult to diagnose the premycotic stage of mycosis fungoides from sections, but from its clinical appearance he regarded the condition in this case as premycotic.

Dr. MUENDE said that unfortunately in the early premycotic stage it was frequently difficult to differentiate the condition from a subacute epidermo-dermatitis. He had removed a piece of skin from this patient after she had had X-ray therapy, and histological examination had only shown some acanthosis, with some para- and hyper-keratosis, and marked intercellular œdema, with the formation, in places, of vesiculettes. In the corium there was small round-celled infiltration with numerous chromatophores. From the appearance of the section alone he felt he was not justified in making a definite diagnosis of the premycotic stage of mycosis fungoides.

Acrodermatitis Perstans : ? Pustular Psoriasis.—R. T. BRAIN, M.D.

L. F., a boy, aged $2\frac{1}{2}$, first attended the skin department of the Hospital for Sick Children, in April 1934, with a history of a septic toe-nail, twice removed, and a persistent scaly patch under the left big toe, of a year's duration. The condition was regarded as a septic paronychia but did not respond to treatment, and in July 1934, a scaly lesion about 3 cm. diameter, with sparse subcuticular dry pustules on its surface, and an undermined scaly edge, was seen in the right palm and a similar lesion on the plantar surface of the big toe. Appearances suggested a mycotic infection; Whitfield's ointment and malachite-green paint were tried without success. In October and November three doses of X-rays were given at two weeks' intervals (one-third pastille dose). No appreciable improvement followed, and in December small pits were noted in some of the nails and the persistent plaques on the right palm and left sole had the red glazed surface also suggestive of psoriasis. Treatment with arsenic by mouth and a tar-and-mercury ointment had no effect. In March 1935 it was noticed that the tonsils were enlarged and septic, and they were removed on April 29. When last seen, May 8, the lesions appeared to be somewhat paler. The Wassermann reactions of both the boy and his father are negative.

Lupus Miliaris Faciei.—ROBERT KLABER, M.D.

This man is aged 26. Nine months ago groups of small red papules appeared on his lower eyelids, with a few isolated lesions on his nose and cheeks. Glass-pressure at this time demonstrated their lupoid character. Since then, the redness has disappeared but there has not been any other conspicuous change, in response to treatment by general ultra-violet light and gold injections.

The patient is otherwise in good health and there is no personal or family history of tuberculosis. The Mantoux reaction, however, was strongly positive, with 0·1 and 0·05 c.c. of $\frac{1}{1000}$ old tuberculin, and still positive with 0·025 c.c.

A microscopic section shows, beneath an apparently normal epithelium, an exceptionally large tuberculous giant-cell system with a large central area of caseation. The capillaries on the periphery are highly congested. No acid-fast bacilli could be found in serial sections.

I believe that lupus miliaris faciei is identical with acne agminata of Crocker and that the congestion which is evident clinically in its early stage relates this condition to the rosaceous tuberculide of Lewandowsky.

Barthelmy's "acnitis," like the papulo-necrotic tuberculide on the extremities, while showing a similar histology, displays more definite clinical necrosis, as it tends to evolve more rapidly.

Discussion.—Dr. GOLDSMITH said that, on the whole, he agreed with Dr. Klaber as to classification. He did not think there was an essential difference between any of the conditions mentioned and papulonecrotic tuberculide. Many of these cases were negative

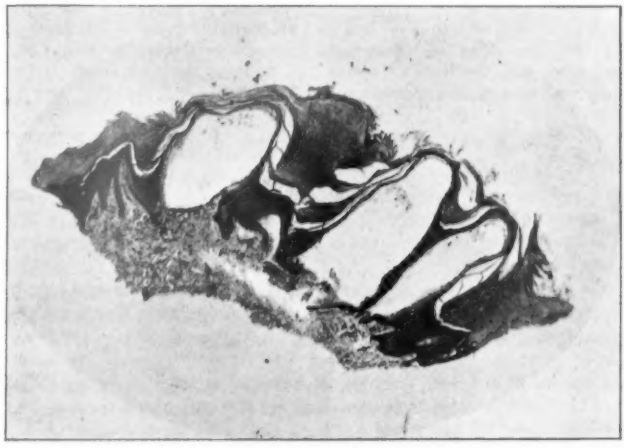
to tuberculin, in which respect they resembled sarcoid, whereas their histology was like that of lupus, though with more pronounced caseation.

Dr. DOWLING said he thought that in lupus miliaris, clinical necrosis was conspicuous by its absence; one only saw occasional pustules resembling acneform pustules.

Angiokeratoma (Mibelli).—ROBERT KLABER, M.D.

The patient is a woman aged 26. Her general health is good, but she has had cold hands and feet as long as she can remember. She suffers from "chilblains" every winter, and even in cold summer weather, on the toes and feet.

There are now on the dorsal—and to a lesser extent, on the plantar—aspect of the toes of both feet, many small scarcely raised angiomata, many of which are surmounted by a hard, warty cap. They are said to have been present for ten years and are not painful or irritable. Those which are not surmounted by a warty growth are seen to consist of grouped purpuric points which only partially disappear



Photomicrograph: Dr. Robert Klaber's case of Angiokeratoma (Mibelli).

under glass pressure. A few isolated lesions, without any evident keratotic element, are also present on the fingers.

I think this case is a classical example of angiokeratoma (Mibelli) which, in its characteristic form, occurs only on a perniotic background. Some diffuse perniosis is now present on the dorsum of the left foot and at the back of the left heel.

I only saw this patient for the first time yesterday, so have not yet had the opportunity of examining a section.

The Mantoux test performed yesterday has so far given only very doubtful reactions.

POSTSCRIPT (1.8.35).—Biopsy has confirmed the diagnosis.

Acrodermatitis Atrophicans Herxheimer.—HUGH GORDON, M.R.C.P.

The patient noticed irritation and the appearance of blotches on the right leg about six years ago.

When first seen, about two years ago, the right leg was much excoriated from scratching. Nearly the whole leg below the knee showed the typical cigarette-paper wrinkling of acrodermatitis atrophicans, with many small nodular infiltrations

which were apparently the site of the irritation. During the last six months the left leg has become involved—considerable irritation being again a prominent symptom. The skin of both legs shows well-marked atrophy, but on the right leg are many small areas of lichenification. If the atrophy were not present the picture would rather resemble that of lichen planus.

The Wassermann reaction is negative.

Report on a section from one of the lichenified nodules (Dr. Robert Klaber). Epithelium shows hyperkeratosis and acanthosis with slight spongiosis. Corium shows œdema. There are many new capillaries showing proliferative changes and surrounded by vacuolated endothelial cells. Weigert's stain shows that the elastic tissue is absent in the infiltrated areas.

Discussion.—Dr. DOWLING thought that the atrophy in this case was senile in type and that the active lesions were lichen planus.

Dr. ROXBURGH agreed that both the hypertrophic lesions and the atrophy were due to lichen planus.

Dr. GORDON (in reply), said that he had had an opportunity of watching the course of the disease on the left leg. The slight atrophy was the first thing noticed, after which came irritation, scratching, and the appearance of the nodules now present. He felt, therefore, that the atrophy was an essential part of the trouble.

Sarcoid of Boeck: Further report on a case previously shown.[1]—HUGH GORDON, M.R.C.P.

When this patient was shown at the meeting held a year ago (March 15, 1934) the earliest lesions were fading, but others were still appearing. There were no fibrocystic changes in the bones; but X-ray examination of the chest showed well-marked peribronchial fibrosis.

The lesions have now almost completely disappeared leaving a fine scarring. The X-ray appearances of the chest are unchanged and the Mantoux reaction is still completely negative.

For the first eight months of last year the patient was given stovarsol by the mouth. She had four courses, each of 36 tablets, with a month's interval between each course. No fresh lesions appeared, and by the end of six months the appearance was much as it is now.

I am showing this patient in the hope of getting some help with regard to the prognosis and treatment of the condition. I am unable to state whether the stovarsol by the mouth did any good in this case, or whether the regression of the lesions was spontaneous, since it had already started before treatment was begun.

I have another patient who has been put on stovarsol, and for a time she undoubtedly improved very much; she has, however, subsequently relapsed. She did not improve on sodium morrhuate injections. So far as I am aware, these patients do not improve on general antituberculous measures or on gold injections, but of the latter I have no experience.

The PRESIDENT said that gold injections effected improvement in some cases of this kind.

[1] *Proceedings*, 1934, xxvii, 1364 (Sect. Derm., 66).

Section of the History of Medicine

President—Sir STCLAIR THOMSON, M.D.

[*December 5*, 1934]

Some Contributions to Mediæval Veterinary Science in the Kitāb al-Falāhah and in Fleta

By TOM HARE, M.D.

MONSIEUR MOULÉ (1896) and Sir Frederick Smith (1919) have shown how, during the eleventh and twelfth centuries, England acquired and developed continental ideas of using the horse for military purposes, for chivalry and for hunting. These ideas created a demand for knowledge of the management of the horse and dog in health and disease. This demand was gradually met by Latin and Norman-French translations of the veterinary works current in the centres of learning in Spain, Sicily and the Mediterranean littoral, which in turn had acquired, through the labours of Byzantine, Semitic, and Moslem writers, the science of Ancient Greece. But in the story of the evolution of mediæval English veterinary science there are many gaps. To bridge some of these I would recommend Mr. Cripps Day's *The Manor Farm* (1931). This treatise on mediæval agriculture inspired me to gather together the following notes which, I believe, amplify, and in some details correct, the histories of Moulé and Smith.

KITAB AL-FALĀHAH

Little is known of Arabic veterinary science preceding the twelfth century. About the end of the thirteenth century the most able Moslem contribution to knowledge of disease of the horse, the *Kitāb al-Nāsirī*, was written by Ibn al-Mundhir al-Baitār, and was dedicated to the Bahrī Mamlūk Sultān, al-Nāsir Muhammad ibn Qalā'ūn, who ruled three times, in 1293, from 1298 to 1308, and from 1309 to 1340. A particular interest is attached to the title of the author. The word baitār is derived from the Greek ἱππιατρός (hippiatros) meaning a doctor of horses, or veterinary surgeon, and ibn al-Baitār thus means "son of the horse doctor." One of the greatest botanists and pharmacists of the Middle Ages was the Spanish Muslim usually known as Ibn al-Baitār. He was born in or near Malaga towards the end of the twelfth century and died in Damascus in 1248.

Sarton (1931) states that the word baitār was used by the pre-Islāmic poets in the sense of leech, and that the baitār was an itinerant doctor of men, as well as of animals, who attended the great fairs or assemblies of the bedouin. Thus it would appear safe to assume that by at least the twelfth century the title baitār was reserved for the veterinary surgeon and that some form of Arab veterinary profession had been evolved.

Some fragmentary evidence as to the evolution of this Arabic veterinary profession is obtainable from the *Kitāb al-Falāhah* (Book of Agriculture) which was

compiled between 1158 and 1200 A.D. by Ibn al-Auwām,[1] who was a Jewish writer living in Seville, which at that time was an important centre for the study of Arabic philosophy. The greater part (30 chapters) of this book of agriculture is devoted to the cultivation of 585 plants and more than 50 fruit trees, to the quality of soils and manures, to the technique of grafting, and to disease of plants. In summarizing the knowledge bequeathed by his predecessors in horticulture, al-Auwām doubtless added his own experience of agriculture in Spain. The last five chapters are devoted to the management of horses, pigeons, and dogs, to apiculture and to animal disease.

Fortunately al-Auwām cites the authorities whence he derived his information. I have summarized such information as I have been able to collect of these authors in the hope of tracing the thread of Arab veterinary learning from the twelfth century back to earlier times.

(1) Al-Auwām states "I have taken as the basis of my work the writings of the wise and illustrious Shaikh Abu 'Umar Ahmad b. Muhammed b. Hajjāj," who was born at Seville and in 1073 compiled the *al-Mukni'* (*al-maqna'* = "The Sufficient"), which was a book of agriculture having many resemblances to the *Geoponica*.

(2) Abu al-Khair of Seville, who is quoted by al-Auwām as the author of a treatise on agriculture. It was suggested to Cripps Day (1931) by H. F. Amendroz that this writer might be either Ahmad b. Muhammed Abu al-Khair al-Ma'arri, the copier of the manuscript on agriculture of Ibn Wahshīya, or a Hammām Abu al-Khair of Seville.

(3) Shaikh Abū Abdallāh Muhammed ibn Ibrāhīm Ibn al-Fassāl, of Andalusia, a writer on agriculture, ? eleventh century.

(4) Gharīb b. Sa'd (Arīb ibn Sa'd al Kātīb al-Qurturbi) a Spanish Muslim historian and physician, who lived at the court of 'Abd al-Rahmān III and of al-Hakam II, at Cordova. In 964-65 he wrote a treatise on gynæcology, hygiene of pregnant women and infants, and on obstetrics (*Khalq al-janīn* = The Creator of the Embryo).

(5) Al-Hājj (or Hadj Ahmed as rendered by Moulé (1896)) of Granada.

(6) Ibn Abi al-Jawād.

(7) Mūsā ibn Naṣr (or Nacr) who is cited 40 times by al-Auwām on diseases of animals.

(8) Ibn Abū Hazem, a writer on equitation, who is cited 150 times by al-Auwām. It is possible that he is the author cited in the *Kitāb al-Nāsirī* (*vide* Moulé, 1896) as Mohammed ibn aki Hizāmi, who lived *circa* 860 under the caliphate of El Moutewakkal. Sarton (1927) gives a brief account of an Abū Yūsuf Ya'qūb ibn akhī Hizāmi who was stable-master to the caliph al-Mu'tadid in Bagdad, 892-902, and was the author of a treatise on equitation (*Kitāb al-furūsīya*), which contained some rudiments of the veterinary art.

(9) Mohaleb ibn Abou Cofarah, who was cited by al-Auwām as a writer on equitation.

(10) Ibn Wahshīya or Abū Bakr Ahmad ibn'Alī ibn al-Wahshiya al-Kaldānī (or al-Nabatī) was born in Iraq of a Nabataean family. He was an alchemist and is the principal authority quoted in al-Auwām's chapters on horticulture. About 904, he compiled from Greek and Byzantine sources the *Kitāb al falāha al-nabatīya* (Book of Nabataean Agriculture) which under the pseudonym of Kūthāmi (or Qutsāmi) he professed to have translated from ancient Babylonian sources. Cripps Day cites Nicholson's conclusion (Lit. Hist. of the Arabs, 1907) that Ibn Wahshīya

[1] Ibn al Auwām's full title has been rendered differently by three authors: viz. Abu Zacaria Jahia aben Mohammed ben Ahmed ebn el Awam, Sevillano (J. A. Banqueri, 1802); Abou Zakaria Jahia ibn Mohammed Abou Ahmed ibn al Awam (J. J. Clément-Mullet, 1864); Shaikh Abu Zakarīyā Yahya b. Muhammad b. Ahmad Ibn al-'Auwām (H. F. Amendroz).

Al Auwām was a contemporary of Moses Maimonides (Abū'l Imrān Musa ibn Maimūn ibn Abdallāh al-Qurtūbi), the Hispano-Jewish philosopher, theologian and physician, who was born in Cordova 1135, and died in Cairo 1204.

perpetrated a forgery by inventing both the name Kūthāmi and the absurdly early date of his authorities. Commenting on the book, Sarton (1927) states that "it contains valuable information on agriculture and superstitions" . . . Wahshīya's purpose "was to extol the Babylonian-Aramean-Syrian civilization (or more simply the "old" civilization before the hegira) against that of the conquering Arabs." . . . "The Nabataeans were the descendants of the old population of Chaldaea and Babylon ; their national language was Aramaic. The term Nabataean was often, however, used, in a conventional and indefinite way, as modern occultists use the term Chaldaean, Coptic or Hindu." Both Moulé (1896) and Smith (1919) were misled by this forgery.

(11) Al-Rāzī (Abū Bakr Muhammed ibn Zakarīyā al-Rāzī) known to mediæval Latinists as Rhazes or Albubator, was a Persian, who was born at Ray, near Teheran in Khurāsān *c.* 850 and died in 923. He was the most celebrated medical clinician of Islam. A student of the methods of Hippocrates and Galen, he became the head of the hospital at Bagdad and was the first to differentiate smallpox from measles and to introduce chemical preparations, e.g. mercurial ointment, into medical practice. Rhazes is credited with about 237 works, including an encyclopædia of medicine and surgery.

(12) Isaac Judaeus (Abū Ya'qūb Ishāq ibn Sulaimān al-Isrā'īlī) was a Jew born in Egypt *c.* 850, and died *c.* 941. He practised ophthalmology at Qairawān in Tunis and became physician to several Egyptian rulers under the eastern caliphate. He wrote several medical works and was one of the first to direct the attention of the Jews to Greek science and philosophy (Sarton, 1927).

(13) Thābit ibn Qurra (or Kurrah) (Abū-l-Hasan Thābit ibn Qurra ibn Marwān al-Harrāni) was born in Iraq 826-27 (or 835-36) and died *c.* 901. He was a physician, mathematician, and astronomer; and founded in Bagdad a school for the translation into Arabic of the Greek authors, particularly of Aristotle, Hippocrates, Galen, Apolonnios, Archimedes, Euclid, Theodosios, Ptolemy and Entocios. In a book on veterinary medicine he states that he drew upon a Persian work (Sarton, 1927).

(14) Ibn Qutaiba (Abū Muhammed'Abdallāh ibn Muslim ibn Qutaiba al Dīnawarī), was born of Iranian stock at Bagdad in 828 or 829. He flourished as a philologist, historian and writer at Dīnawar and later at Bagdad, where he died *c.* 889. Among his works are *Kitāb al-ma'ārif* (Book of General Knowledge) and *Kitāb adab al-Katīb* (Accomplishments of the Secretary) ; in the latter he wrote upon the external conformation of the horse.

(15) Abū Hanīfa Ahmed ibn Dā'ūd al-Dīnawarī was born at Dīnawar in Iraq probably between 815 and 825 and died *c.* 895. He was the author of *Kitāb al-nabāt* (Book of Plants).

(16) Al-asma'ī (Abd al-Malik ibn Quraib al-Asma'ī) was a true Arab, born at Basra in 739-40. He flourished at Bagdad and Basra, where he died *c.* 831. He was one of the greatest Arab scholars of his time, and the rival of Abū'Ubaida (q.s.). He wrote many works of an anecdotal character, e.g. on the horse (*Kitāb al khail*) the camel (*Kitāb al-ibil*), wild animals, (*Kitāb al-wuhūsh*), sheep (*Kitāb al-sha'*) and on the making of man (*Kitāb khalq al-insān*).

(17) Abū'Ubaida (Abū'Ubaida Ma'mar ibn al-Muthannā) was a Persian Jew born in 728 at Basra, where he died *c.* 825. He was a celebrated historian, philologist and scientist.

Al-Auwām states: "I have also introduced into the work anything of value attributed to the following learned men, Dīmwāt, Galen, Anatolius of Africa, certain Persian authors, Kastos, Kassius, Aristotle and Makarius the Greek."

It appears to be widely assumed that al-Auwām wrote Dīmwāt in mistake for Buqrāt, the Arabic abbreviation for Hippocrates of Cos, whose works, together with those of Dioscorides, were certainly handed down by some of the Muslim authors quoted in the *Kitāb al-Falāhah*. I think it worthy of mention at this point that in

the generation following al-Auwām's there was born (in 1217) on the island of Tunā, near Dimyāt (Damietta) the traditionalist 'Abdal-Mu'min al-Dimyātī (Abū Muhammad 'Abd al-Mu'min ibn Khalaf; or Sharaf al-dīn al-Tūnī al-Dimyātī al-Shāfi'ī). He died in 1306, leaving as his main work a collection of traditions concerning horses, *Kitāb fadl al-khail* (excellence of horses). This book is divided into 8 chapters which are entitled: (1) The merit of horses used in the jihād (Holy War). (2) The castration of horses, a forbidden thing. (3) The choosing of horses, the colours to be preferred. (4) Markings of evil omen. (5) Competitions for prizes are forbidden, except with regard to horses and camels. (6) Spoils belonging to the rider. (7) Muslim horses free from taxation. (8) Names of the Prophet's horses.

Anatolius of Africa or Vindonius (or Vidiamus) Anatolius of Berytos (i.e. Beirut) in Syria, during the fourth century wrote a treatise on agriculture, from which Cassianos Bassus, a Byzantine lawyer compiled the *Geoponica* in the sixth century. According to Sarton (1927) the Byzantine *Geoponica* was translated into Syriac by Sergios of Resaina (first half of the sixth century) and the Syriac version was in its turn the basis of an Arabic adaptation by Qustā ibn Lūqā al-Ba'labakkī (i.e. from Baalbek or Heliopolis, in Syria) who was a Greek Christian physician, philosopher, astronomer and mathematician, and flourished in Bagdad, dying in Armenia *c.* 912.

There appears to be no justification either for Moulé's suggestion (1896) or Smith's positive statement (1919) that al-Auwām quoted the hypothetical author "Hippocrates the veterinarian."

If an analysis of al-Auwām's authorities enables us to trace something of the evolution of twelfth century Arab knowledge of horticulture, of botany, of pharmacy and of medicine, it leaves us in some doubt about the evolution of Arab veterinary science. It is to be hoped that scholars will endeavour to track down the three chief authorities for al-Auwām's statements on animal diseases—viz. Musa Ibn Nasr, Ibn Abū Hazem, and Mohaleb Ibn Abou Cofarah. Apparently these three writers lived at least some two to three centuries before al-Auwām. Were they mere compilers or transcribers like Thābit ibn Qurra, Ibn Qutaiba and Al-asma'ī, who in the ninth century collected veterinary information from earlier authors, or were they personally experienced in the veterinary art? By the ninth century the medical profession of the Eastern Caliphate was furnished with hospitals and training schools, and some Arab physicians had already established their permanent place in history. Was the Arab horse-doctor (baitār) existing at this time, or was he yet to be evolved from the itinerant leeches (of the pre-Islamic poets) into the baitār of the twelfth century, when the horse as an index of social position and as an instrument of power had acquired value in an all-powerful Arab dominion?

It is well established that the great flood of Greek and Byzantine science flowed through Syriac via the Greek school of Alexandria into the Arabic of the eastern Caliphate, where it was joined by such tributaries as the astrology and pharmacy of Assyro-Babylonian medicine. Thence it was directed by Jewish scholars to their academy at Cordova (founded in 960) on to Toledo and other seats of Jewish translations in the Iberian peninsula to the Latin west. So we recognize that on account of some 500 years of Moslem industry, principally through intellectual Jewish subjects, the veterinary science of ancient Greece was recovered for, and transmitted to, mediæval Europe.

Stupor Mundi

The *Kitāb al-Falāhah* of al-Auwām was cited by Jordanus Ruffus in his work on equine medicine, which exerted a profound influence upon the veterinary science of mediæval, and even of modern, Europe. Ruffus was "Senior Imperial Marshal" of the Stupor Mundi (Frederick II, King of Sicily and founder of the University of Naples in 1224, born 1194, died 1250).

Another source of information cited by Ruffus was the Arabic treatise on veterinary medicine, which in 1277 was translated into Latin, under the title "*De curationibus infirmitatum aequorum*," by the Jewish-Sicilian scribe, Moses of Palermo (Moses Panormitanus) on the instructions of Charles of Anjou (King of Naples and Sicily, 1266 to 1282). The Arabic compiler of this work had attempted like many of his contemporaries, to foist its authorship on to Hippocrates (the Father of Medicine) by using the title "Ippocras." In seeking an origin for the treatise Smith (1919) was misled into assuming that "Ippocras" was a native of India, who was employed by Chosroes (King of Persia, 531 to 579) to write a book on the diseases of the horse.

Fleta

By reprinting *Fleta* in his book, Cripps Day (1931) has earned the gratitude of veterinary historians, who hitherto have overlooked this interesting thirteenth-century English treatise on agriculture. According to Cripps Day, *Fleta* was written about 1289, probably by a lawyer. It was transcribed in the reign of Edward II by Selden, whose MS. (preserved in the British Museum) was printed in London in 1647, the second edition following in 1685.

A large proportion of the contents of *Fleta* was abstracted from Walter of Henley's *Hosebonderie* (written *c.* 1221) and from the *Seneschaucie* (written in the reign of Edward I) which was an anonymous tract on the administration of a manor. But *Fleta* also drew upon other and as yet undefined sources for some of his instructions; for example, those upon the duties of the mareschal are not in *Hosebonderie* or *Seneschaucie*.

Chapter 74, section 1. "The duty of the mareschal is to take a tally of the provender with the provost, and to record every night the number of guests' horses in the day's account so that he may insert the number of horses in his roll for the seneschal specifying the names of those that are present, when they came, and the length of their stay."

Chapter 74, section 2. "Item, to receive bran, when necessary, from the provost by tally, and to render an account thereof to the seneschal and as with the bran, so with the oats."

Chapter 74, section 3. "Item, to take a tally from the provost of horseshoes and nails received from him and to inform the seneschal both of the number of horseshoes, and of their cost, and how he shall have used them; nor must he allow other people's horses to be shod without his leave. Item, to give out hay and litter for the horses."

Chapter 72, section 17, instructs the seneschal "to account every night on the lord's behalf for the expenses of the household, with the buyer, mareschal, cook, the chief officer of the buttery and other officers and to ascertain the total of the day's expenses."

Dr. Bullock (1929) described the manner in which the title of mareschal or marshal was sometimes applied in England to the doctor of animals. Bullock found the earliest reference to the title in *Wace's Chronicle* of 1330. *Fleta* defines the mareschal as an officer of the manor, who is directly responsible to the seneschal or chief officer for the management of the horses and of the smithy. Whence did *Fleta* obtain these definitions of the mareschal? *Fleta's* definitions differ from those given for the mareschal in *Les Reules Seynt Roberd* (*c.* 1240), which was written by Robert Grosseteste (*c.* 1175 to 1253), Bishop of Lincoln. But it is possible that Robert Grosseteste introduced the title of mareschal into England, since, as Kington (quoted by Cripps Day) points out, Grosseteste was among the correspondents of the Stupor Mundi, whose "Senior Imperial Marshal" was the celebrated veterinary author, Jordanus Ruffus. Between the writing of the work

by Ruffus and the writing of *Fleta* there was time for the introduction to Englishmen of the Stupor Mundi's notions of the mareschal's duties.

During the thirteenth century in England the mareschal was the master of the horse. There is no evidence that he was required to doctor the horses or other animals of the manor, neither was he required to conduct post-mortem examinations as shown by the next extract from *Fleta*.

Chapter 72, section 16. "He [the Seneschal] must make rule that no sheep or beast belonging to the lord should ever be skinned, even under special circumstances, before it has been seen by the bailiff and provost and other trustworthy people so that the cause of its death may be ascertained, because it may have died from various causes, such as being killed or strangled by some one, lost, stolen, maimed, or injured and the like, through being improperly looked after, in which cases the lord ought to be completely indemnified. But if it died from a cause which could not have been foreseen, from fire, accidental drowning or maiming, old age, and the like, the man in charge ought not to be held liable; . . ."

It is evident from the following two sections, which had been extracted from *Seneschaucie* that the origin of "liver rot" or fluke disease [distomatosis] in sheep was related to white snails in the thirteenth century.

Chapter 79, section 3. ". . . he [the shepherd] must be careful that the sheep in his charge are not stolen or changed, nor allowed to graze in wet or marshy places, in thickets, or on low-lying bottoms, or unhealthy pastures, lest, for want of good care, they go sick and die. . . ."

Chapter 79, section 15. ". . . between the two feasts of the Blessed Mary in August and September they [the sheep] may have got the rot and become diseased by being wrongly put on bad pasture, or by swallowing a certain rime which then falls, or by eating white snails."

Smith (1919) attributed this discovery to Fitzherbert whose *Boke of Husbandry* (*c.* 1523) contained a description of the symptoms of the disease and of the lesions in the liver as "little live things like flokes in the liver, full of knots and white blisters." Fitzherbert repeated the view recorded in *Fleta* that ill-effects result in sheep which are grazed on the mildewed grass of autumn. The "rime" (mildew) of *Fleta* appears to have been the "yrignée" or "iraignée" of French mediæval agriculturalists (toile d'araignée or spider's web) and it gave rise to the name of the ovine disease "yrengnier," which was described by Jehan de Brie in 1379. According to de Brie, yrengnier followed the eating of a mildewed clover ("muguet saulvaige") and was characterized by swelling of the sheep's body (? ascites) and by the escape of a yellow-coloured serum on slitting the ear or skin of the muzzle (? jaundice).

By the final four words of the following section *Fleta* exhibits more caution and accuracy than many present-day sheep farmers who firmly believe that wool in their stomachs causes the death of lambs.

Chapter 79, section 8. "When the ewes begin to drop their lambs, the shepherd must remove any wool from about the udders of the mothers, lest their lambs swallow the wool on the udder when sucking and die from the wool remaining in their stomachs, which is quite possible."

In the following sections, which were extracted from *Hosebonderie*, *Fleta* gives information which was repeated by many writers of later times.

Chapter 79, section 7. "It is best to keep the sheep under shelter at night between Martinmas and Easter, unless the ground is dry, the fold well kept and the weather mild. In that case it is perhaps expedient to fold the wethers, but hay must be given to the weakly ones kept in the cote; but if, owing to bad weather, the wethers are kept in the cote, they should be kept separate, and coarser hay with oat and wheat straw, well thrashed, given to them. For if they are disturbed at night or in the morning by a storm, and consequently have eaten little or nothing, then

afterwards when they are put out hungry in the enclosure and find unmixed hay, they will not eat it properly, but swallow it down whole, and as their nature is to ruminate, what has not been chewed will not come to the cud, and it is possible such sheep may die from the fermenting of that hay remaining in their stomachs; it is therefore good to mix straw with the hay, so that they may be obliged to chew the hay because of the coarseness of the straw."

Chapter 79, section 13. ". . . it is good to have the sheep viewed three times a year by experienced men, and at once sell unsheared those suffering from inflammation, the sick and diseased ones (these may easily be recognized by their wool coming off the pelts, their yellowish eyes, and diseased teeth); . . ."

The term "struck" is commonly applied by present-day sheep farmers to any acute fatal infection of rapid onset. Mediæval England used an equally ambiguous term "murrain" for contagious infections of horses, cattle and sheep. Smith (1919) suggests, on very slender evidence, that it was anthrax.

Chapter 79, section 16. "When a sheep is reported as dead, and it is found to have died of the murrain, sickness, or some other known cause, the thing to be found out is whether it was before or after shearing." (Extracted from *Seneschaucie*.)

Chapter 79, section 6. ". . . some careful people have the flesh of those [sheep] dying of murrain put into water for the period between the hour of nine and vespers, and afterwards hung up so that the water drains off; the flesh is afterwards salted and dried and they are made worth something and can be distributed among the workpeople and the household; . . ."

This extract from *Hosebonderie* reminds us that "by mediæval regulations in London, at Oxford, and in Scottish boroughs, the meat condemned as putrid by the supervisors of the market was confiscated and given to hospitals." (Coulton, 1926.)

Fleta also repeats the sound advice given by *Hosebonderie* and *Seneschaucie* on the management of cattle and calves, from which the following sentence is abstracted: "After weaning, let them [calves] have plenty of water, both indoors and out, lest, for want of water, as frequently happens, they die of lung disease." (*Fleta*, Chapter 76, section 10).

In Chapter 83, *Fleta* defines the duties of the baker of the manor, who "must not make any issue of bran for dog's food or for bread for the men-servants or for the poor . . ." which indicates that mediæval hounds subsisted, like working sheep-dogs of the present-day farm, mainly on a farinacious diet.

Chapter 71, section 9, refers to "fines and penalties in connexion with the lawing of dogs." Cripps Day (1931) states that this section in *Fleta* was taken from the statute *Extenta Manerii* (4 Edward I) and that the term "lawing" was defined as the amputation of the claws and balls of the dog's forefeet. The statute "was first used in the Assize of Woodstock (K. Hen. II)." Under the stringent Forest Law of the Norman and Plantagenet kings the owners of holdings within the royal forests were only permitted to keep such dogs as had been "expeditated" (i.e. lawed) or "hoxed" (i.e., hamstrung). The operation of lawing was performed with hammer and chisel.

From the description in *Fleta* of the mareschal as the master of horse, and from the finding that Robert Grosseteste corresponded with Frederick II of Sicily, it would appear reasonable to conclude that by the middle of the thirteenth century England was making contact with some of the veterinary science as practised in more enlightened Mediterranean countries. But many years were to pass before the English mareschals and farriers had assimilated, and written their own books upon, the veterinary science of the East.

Before this influx, however, thirteenth-century England was not ill-equipped with ideas on the management of sheep and cattle in health and disease. The extracts from *Hosebonderie* and *Seneschaucie* possess an original character; they, as the description of liver-rot in sheep shows, were the observations of men in lands

which were silvered with the autumn rime. Probably they were the one part of mediæval English veterinary science which was indigenous—a product of the progressive sheep industry which was prosperous even in Anglo-Saxon England. Gradually these indigenous ideas were refined, though never displaced, by the importation and assimilation of a science which evolved in Ancient Greece.

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An F. Baker Snuff-Box Belonging to an Eighteenth Century Apothecary

By TOM HARE, M.D.

[*April* 8, 1935]

I AM exhibiting one of my pressed-horn snuff- or tobacco-boxes. This oval box is $3\frac{3}{4} \times 2\frac{3}{4}$ in. $\times$ 1 in. high, with a detachable lid $4 \times 3\frac{1}{5} \times \frac{3}{5}$ in. The lid bears in relief the arms of the Lumber Troop, the design for which was probably taken from an engraving by Hogarth (fig. 1). The arms comprise a punch-bowl between a moon and a six-pointed star in chief, a lantern in base, with Mercury and Ceres as supporters; the crest is an owl standing on a barrel; and the motto is "In Nocte Laetamur."

According to an article in *Old and New London*, vol. i, pp. 114, 116 and 117, the Lumber Troop was an eighteenth century club, which in the later part of its history met in Dr. Johnson's house in Bolt Court off Fleet Street. It is recorded of the Troop in the early nineteenth century that "they are a respectable smoking club, well known to every candidate for a seat in Parliament for London, and famed for the quality of tobacco they consume and the porter they drink. . . ."

E. Jackson Barron, Esq., presented to the London Museum a case of relics of the London Troop comprising: (1) A box similar to the present exhibit (A. 14564); (2) an oval box pressed from a different die (A. 14565); (3) the treasurer's key; and (4) the president's or sutler's badge (A. 14562). The president's badge depicts a panelled room, at the back a shelf carrying three toy cannons over a window, before which is a circular table covered by a cloth, two wine glasses and one pewter tankard. Four men are seated at the table, of whom one holds a churchwarden clay pipe and another holds a pewter tankard, a servitor bearing a punch bowl enters from a door on the right. The badge is inscribed "Ireland. Sutler", suggesting the possibility of an Irish branch of the club.

The rimless pressed-horn lid of an oval box bearing the arms of the Lumber Troop was presented by Lady Charlotte Schreiber to the British Museum (Plaquette room, case No. 23). A box, similar to mine, was shown at the Exhibition of British Art 1934, at Burlington House (*vide*, exhibit No. 1593 in the Commemorative Catalogue of British Art, London, 1934).

I have obtained no record, beyond his name, of the artist craftsman, who produced these boxes in the manner of John Obrisset (active in London *c.* 1685-1728). The words "F. BAKER. FECIT" are pressed on the lid beneath the motto (fig. 1). I

FIG. 1.—Photograph of the lid of the snuff-box showing the arms of the Lumber Troop.

FIG. 2.—Photograph of the base of the snuff-box showing John Graham's inscription.

am indebted to E. B. Nichols, Esq., Clerk to the Worshipful Company of Horners, for the information that the Company's charter of 1638 bears the name of Robert Baker as the first master. Moreover, for many years during the second half of the seventeenth century the roll of masters of the Company bears the name of Baker,

but makes no mention of F. Baker. Mindful of the tendency for such a specialized and restricted craft as horn-working to be handed from father to son I think it not unreasonable to suggest that F. Baker was probably a relative of the seventeenth century masters of the Horner's Company.

The unusual feature of the box which I am exhibiting is the inscription on its base "Jno Graham Apoth. Carlile" (fig. 2). I am indebted to the Town Clerk and the District Probate Registrar of Carlisle for the information that a tombstone in the disused burial-ground of St. Cuthbert's church in their city is inscribed "John Graham, Apothecary of Carlisle, died 25th June 1757 aged 49". There is also a record that the administration of John Graham's estate was granted to his widow, Mary Graham, in November 1757.

Thus it is almost certain that John Graham's box was made during his lifetime and that F. Baker was active before 1757. Connoisseurs may not regard Baker's work as equal in quality to that of Obrisset, but, in my opinion, it is of sufficient merit to warrant our recognizing F. Baker as a distinguished English artist-craftsman of the first half of the eighteenth century.